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30

Annotation

A genetic model compatible with a dimensional view of schizophrenia. *D. Roberts and G. Claridge* 451

Review Article

"Life, Jim, but not as we know it"? Transmissible dementias and the prion protein. *P. J. Harrison and G. W. Roberts* 457

Papers

Evidence for allelic heterogeneity in familial early-onset Alzheimer's disease. *C. M. van Duijn, C. van Broeckhoven, J. A. Hardy, A. M. Goate, M. N. Rossor, A. Vandenberghe, J-J. Martin, A. Hofman and M. J. Mullan* 471

Social deprivation and rates of treated mental disorder. Developing statistical models to predict psychiatric service utilisation. *G. Thornicroft* 475

A retrospective case-note study of bipolar disorder in old age. *J. Snowdon* 485

Bulimia nervosa: family size, sibling sex and birth order. A catchment-area study. *J. H. Lacey, S. G. Gowers and A. V. Bhat* 491

Anorexia nervosa: outcome and prognostic factors after 20 years. *R. H. Ratnasuriya, I. Eisler, G. I. Szmukler and G. F. M. Russell* 495

The effects of clozapine on tardive dyskinesia. *J. A. Lieberman, B. L. Saltz, C. A. Johns, S. Pollack, M. Borenstein and J. Kane* 503

A double-blind comparison of the effects of gradual withdrawal of lorazepam, diazepam and bromazepam in benzodiazepine dependence. *S. M. Murphy and P. Tyrer* 511

Management of first episode psychotic illness in Afro-Caribbean patients. *E. Y. H. Chen, G. Harrison and P. J. Standen* 517

Psychotic depression: psychoanalytic psychopathology in relation to treatment and management. *C. Lund* 523

Early cortical tactile-evoked potentials, laterality and schizophrenia. *J. E. Allen, A. Jenner and J. C. Stevens* 529

Auditory selective attention and event-related potential in schizophrenia. *P. B. Ward, S. V. Catts, A. M. Fox, P. T. Michie and N. McConaghy* 534

Unfit to plead in England and Wales, 1976–88. A survey. *D. H. Grubin* 540

Prevalence of delusional jealousy in different psychiatric disorders. An analysis of 93 cases. *M. Soyka, G. Naber and A. Völcker* 549

Psychiatric screening of admissions to an accident and emergency ward. *G. Bell, D. Z. Reinstein, G. Rajiyah and R. Rosser* 554

The Current Literature

Effect of central cholinergic stimulation on regional cerebral blood flow in Alzheimer's disease. *K. Wilson, D. Bowen, P. Francis and P. Tyrrell* 558

Continued inside

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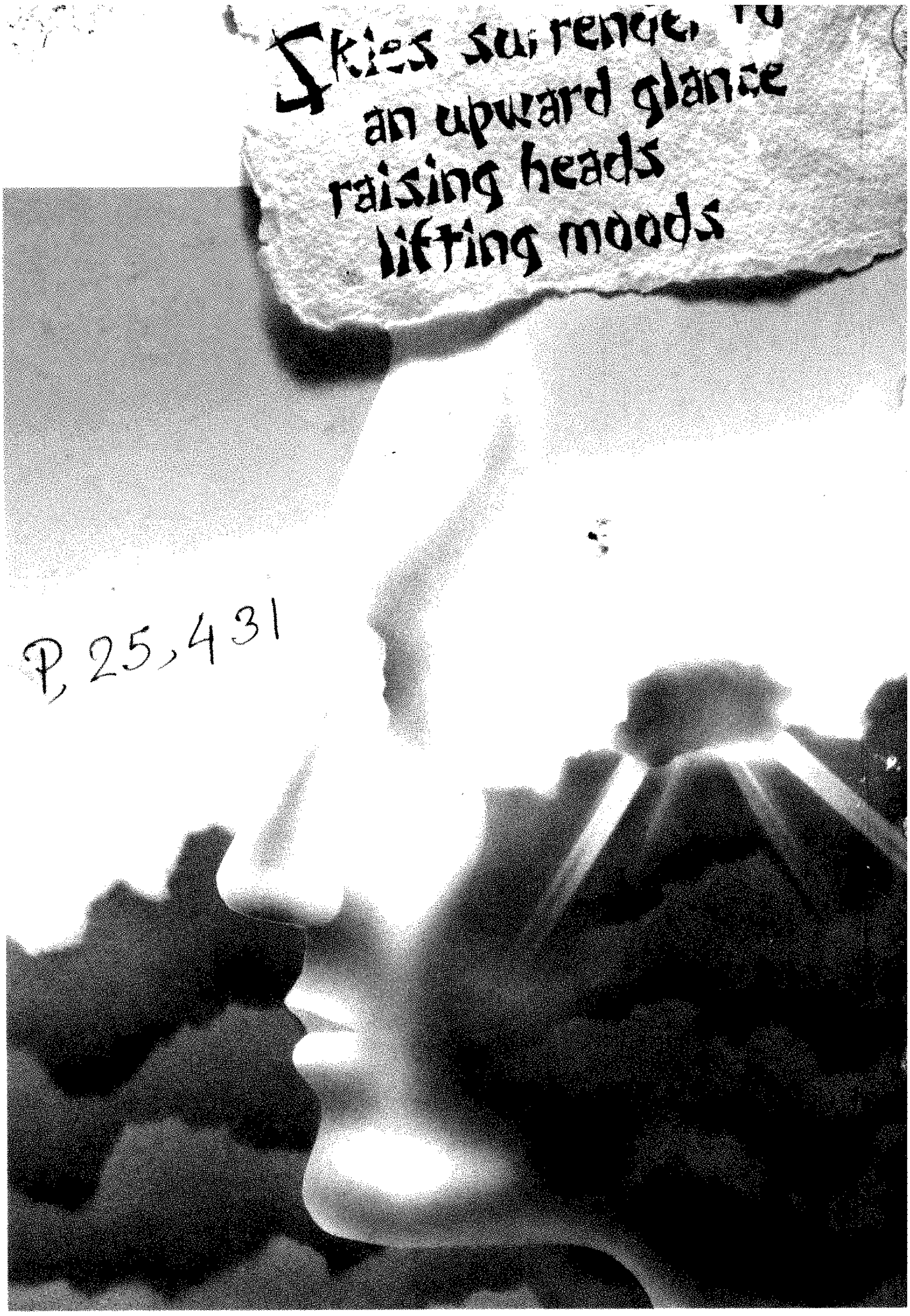

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Contents continued from front cover

Point of view

The functional psychoses – are oncogenes involved in their pathogenesis? Some speculations. *J. Leach* 563

Columns

Correspondence 569
A hundred years ago. *Researched by H. Rollin* 578
Reading about... Transcultural psychiatry. *J. L. Cox* 579
Book reviews 583
American Journal of Psychiatry (contents) 592
The Journal of Nervous and Mental Disease (contents) *facing* 592

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Annotation

A Genetic Model Compatible with a Dimensional View of Schizophrenia

DAVID ROBERTS and GORDON CLARIDGE

Throughout the history of schizophrenia as a psychiatric concept, opinions have differed sharply over its essential nature and its causes, giving rise to a wide range of explanations that have drawn upon ideas from almost all of the social and biological sciences. Only one fact has truly survived the vicissitudes of argument about the condition: that genetic factors contribute to its aetiology. Even that conclusion, first reached in the very early days of schizophrenia research, sank temporarily out of sight during the radical psychiatry challenges of the 1960s. However, the continuing collection of family, twin, adoption and other data over that period put the genetic hypothesis beyond reasonable doubt (McGuffin, 1988).

Despite the virtual certainty of the genetic involvement, the mode of inheritance in schizophrenia is still unknown. Most discussion has revolved around the 'single-gene' models *versus* the 'multifactorial-polygenic' models (Gottesman & Shields, 1982). Preference for one or other of these theories has generally reflected the view taken of schizophrenia itself and the role that particular writers have seen for heritable factors in the cause and course of the disorder. This in turn has coincided roughly with opinion about schizophrenia *vis-á-vis* its status as a disease. Those who have adopted a traditional medical model view of schizophrenia – i.e. most organic psychiatrists – have tended to prefer some form of single-gene explanation of its inheritance, presumably on the grounds that, if true, it would provide the most parsimonious account of what is perceived as being a brain disease, in the classic sense. Polygenic theories, on the other hand, have been especially popular among those – mainly psychologists – who have construed schizophrenia in more dimensional terms (Meehl, 1962; Eysenck & Eysenck, 1976). According to the latter view, schizophrenia, while being a gross aberration of mental functioning, is nevertheless in some respects continuous with the normal state, where its milder characteristics are manifest as schizotypal personality traits (Claridge, 1987, 1988).

Fresh impetus has been given to the above debate by the advent of the so-called 'new genetics', which offer techniques that might, in principle at least, settle such issues (Pato *et al*, 1989). So far the application of the procedures of the 'new genetics' in psychiatry has been driven by a belief in major gene theories of mental illness. Indeed, their use forms only part of an increased research effort, particularly in the neurosciences, to understand the biology of the functional psychoses, accompanied by a growing optimism that those disorders can at long last be established as genuine neurological diseases (Crow, 1987). Consequently, in some quarters at least, alternative perspectives on psychosis, including schizophrenia, have come to seem less persuasive. That this should be mirrored in expectations about the potential contribution of genetics is not surprising: discovering a gene responsible for schizophrenia becomes a logical aim, the prospect of finding it gives immediate cause for hope, and the search for it a manageable undertaking. In contrast, polygenic theories appear vague, difficult to test in the foreseeable future, and in any case largely sustained by, and employed to sustain, a view of schizophrenia that is unfamiliar to most psychiatrists.

The current ascendency of neurological disease theories of schizophrenia should not however be taken to mean that they are now beyond scrutiny or that alternative models have lost their credibility. On the contrary, as we hope to show in this paper, the genetics of schizophrenia, and therefore how we construe it as a disorder, are matters that are still open to debate, with the dimensional view still very much in play. In this respect, and to introduce our discussion, the following point is worth making. Much has been written on the genetics of schizophrenia and many models have been proposed (see Gottesman & Shields, 1982; Gottesman *et al*, 1987; McGuffin, 1988). At first glance, some of the evidence appears to be contradictory: one gene *versus* many, a dominant mutation *versus* a recessive one, a gene on chromosome 5 *versus* a gene not on chromosome 5 (Sherrington *et al*, 1988; Kennedy *et al*, 1988), etc. Similarly, there is debate as to whether schizophrenia is a single complaint or embraces many different complaints and whether schizophrenia and schizotypy have the same basis. There is also dispute as to the role of the environment, the issue here being especially confused by the ambiguous nature of the twin data: monozygotic twins, although showing higher concordance than dizygotic twins, do so to varying degrees in different studies.

While often not appreciated, the fact is that the findings so far from the 'new-genetics' research on schizophrenia are actually neutral with regard to the old debate about whether one gene or many genes are involved: *both* the single-gene theories *and* polygenic theories of inheritance are contradicted by the evidence. For the moment, therefore, the choice of working model for the genetics of schizophrenia continues to rest on inspired guesswork, based on a judgement as to which mechanism of inheritance is compatible with other reasonably attested facts about the condition and on what is known of the genetic control of other complex biological phenomena.

Here we shall propose a model drawing on well established principles which, as far as we are aware, have not hitherto been considered in the psychiatric literature. The model was inspired by an attempt to construct a feasible explanation of the genetics of schizophrenia that could be taken beyond the conventional polygenic theory while still being consistent with a dimensional view of the disorder.

As our starting point, rather than taking the genetic observations on schizophrenia, we have, instead, considered a reasonable model for the genetic control of the development and maintenance of brain function and mental activity and then addressed how changes in this might lead to traits of schizotypy and, in more extreme cases, to symptoms of schizophrenia. The general assumptions of the model are as follows.

- (a) Brain function and mental activity are the end-product of a number of different pathways with steps in the pathways controlled sequentially by different gene products.
- (b) A block in at least one of these pathways can lead to the symptoms of schizophrenia.
- (c) Mutations in different genes controlling successive steps in the pathway can lead to the same block.
- (d) Different mutations of the same gene can have different phenotypes.
- (e) There are gene–environment interactions.
- (f) There are gene–gene interactions.
- (g) There is a threshold level of normal gene product required for normal functioning.

A paradigm case of this kind of model is that first put forward by Beadle & Ephrussi (1937) to explain the genetics of eye colour in *Drosophila*. The normal eye colour of the fruit-fly *Drosophila* is the end-product of a multistep pathway as illustrated in Fig. 1.

Each step is controlled by the product of a gene, in this case an enzyme. The complete loss of any one of the gene products, due to gene mutation, will mean the loss of the end-product and will result in abnormal eye colour. In fact, the normal eye colour, red, is the product of a number of pigments, the scarlet pterins and the brown ommochromes. Thus several different mutations affecting xanthomatin synthesis results in the failure of brown pigment and

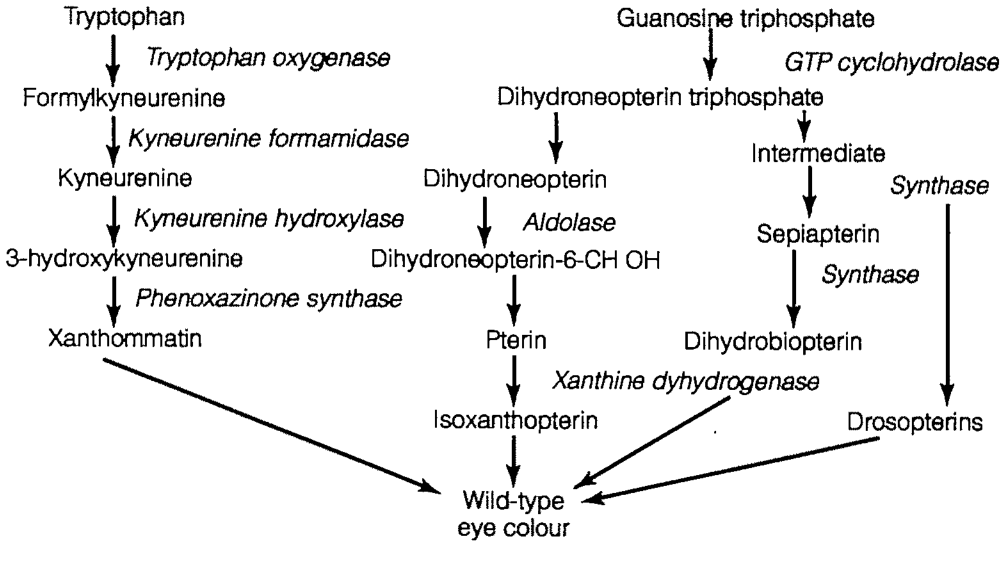

Fig. 1 Synthesis of wild-type eye colour in *Drosophila* (after Summers *et al*, 1982) (enyzmes shown in italic).

flies with scarlet eyes. Similarly, mutations in the other pathways lead to flies with brown eyes. Blocks in both pathways result in no pigment being formed, giving the fly white eyes.

In a like way, a single pathway or the interaction of a number of pathways gives rise to the secondary sexual characteristics (Nöthiger & Steinmann-Zwicky, 1985), the dorsoventral axis (Anderson, 1987) and the segmental values in *Drosophila* (Akam, 1987). An example, to be discussed later, of a similar pathway in man is the control of blood clotting, with a block of any step in the pathway preventing normal blood clotting, leading to symptoms of haemophilia (Ratnoff, 1978).

An important feature of our argument concerns the nature of point mutations, which can be of two kinds. The first leads to the complete lack of activity of the gene product and is frequently a null mutation in which no product is made. These mutations can be deletions of the gene, an alteration in the coding sequence generating a chain-terminating codon that may generate an unstable truncated gene product. The complete lack of activity can also be due to an altered amino-acid sequence, leading to the synthesis of an abnormal protein which fails to fold correctly to give the active site.

The second class of mutation is the 'leaky' mutation that retains a residual level of biological activity. These leaky mutations are the consequence of an altered amino acid leading to an alteration in protein structure. The residual activity is either because the normal amount of protein is synthesised but each altered molecule has a reduced biological activity, or because the molecules have normal activity but the mutation makes them unstable, leading to a shorter half-life and a reduction in the amount present.

Mutations of the first class would lead to a complete block in the pathway. When the product of a mutant gene lacks all activity and the mutation is recessive, the organism copes with 50% of the normal activity. (There is evidence that within quite broad limits the amount of gene product is strictly proportional to gene dose (Roberts *et al*, 1984).) However, when the organism is homozygous for the mutant allele (i.e. wth 0% activity), then the mutant phenotype is manifest. Somewhere between 50% and 0% activity is a threshold. Values below this threshold result in the mutant phenotype. It is unlikely that it will be a sharp cut-off but rather an increasing severity of the mutant phenotype as the level of active gene product decreases. In the present case this would be represented as a continuum ranging from schizotypic traits through to the clinical symptoms of schizophrenia.

Let us suppose that schizophrenia results from defects in a pathway $a \to b \to c \to$ brain function. A complete (i.e. non-leaky) mutation in the gene controlling the step $a \to b$ or a similar mutation in the gene controlling the step $b \to c$ would have exactly the same phenotype, the failure of development of brain function being manifest as schizophrenia. In other words, there may be a gene which can mutate to give schizophrenia on chromosome 5 and another on a different chromosome. Indeed, there may be several.

Suppose we have a complete mutation of the gene controlling the step $a \to b$. The heterozygote would produce on average 50% of the active protein. Suppose the threshold requirement for this protein to be 40% of the normal level. There will be cases, due to environmental differences, where individuals heterozygous for the mutant gene fall below this threshold and manifest schizophrenia. In this case the mutant would be dominant but with incomplete penetrance. The same variation in environmental conditions would, for example, allow one of a pair of monozygotic twins to fall below the threshold manifesting schizophrenia while the other would be above the threshold, and clinically normal.

Depending on how close the threshold is to the 50% level then there will be greater or less discordance between monozygotic twins. Moreover, the degree of concordance will vary depending on which gene is mutated and which mutant allele is under consideration. Collating all twin data would be meaningless unless like were considered with like; that is, only monozygotic twins all carrying the *same* mutant allele can be collated. For although the phenotype is the same, the genetic basis is quite different.

With the exception of monozygotic twins, the genetic background will also contribute to the variation in protein activity and, as this genetic contribution will vary from family to family, so in some families a large number of heterozygotes will manifest, while in other families few will manifest, the complaint. If the threshold is very low then rarely, if at all, will any heterozygote fall below the threshold. In that case the mutation would be recessive.

A leaky mutation acts similarly. In the heterozygote there will on average be 50% of the normal activity from the wild-type chromosome and some extra activity from the defective gene. In the homozygous mutant there will be two doses of the defective gene and whether these produce a level of activity above the threshold level or not will govern the manifestation of schizophrenia. The final levels will again be controlled by environment and genetics.

These cases explain the variation in the penetrance of schizophrenia and the apparent contradiction in the data from monozygotic twins. They also show how mutations of some genes can be dominant while mutations of others are recessive, yet both having the same phenotype of schizophrenia.

The considerable variation in the symptoms associated with schizophrenia even within families can also be explained, since our model predicts such variation. It is unlikely that the threshold discussed above will be a sharp one. Instead it is likely that individuals with over 50% of normal activity will not show schizophrenia; individuals with, say, 40–50% will show schizotypic traits; below 40% increasingly severe symptoms of schizophrenia will be apparent. A very leaky mutant might have exceptionally mild symptoms while complete mutants will have severe symptoms; the levels will be controlled by the genes and the environment. So, again, members of the same family or even a pair of monozygotic twins can reveal different schizophrenic symptoms.

Different mutations of the *same* gene, or different mutations of different genes, in the pathway leading to schizophrenia could be associated with very different symptoms. We would also expect that the symptoms associated with the *same* mutation would vary with the environment and with the genetic background; other genetically controlled personality characteristics would be an example of the latter.

It is reasonable to ask whether or not there are any known human systems that reflect these principles. One system that has been studied from the genetic and biochemical points of view and which echoes many of the features of our model is blood clotting. A modified version of the intrinsic and extrinsic pathways of thrombin formation is shown in Fig. 2.

The clotting time of whole blood is a measure of the efficiency of this system and in the population this value is distributed normally, with very few individuals showing extreme values. This normal distribution, which is controlled by the environment and by genetic background, may be considered equivalent to schizotypic traits, with only the extremes

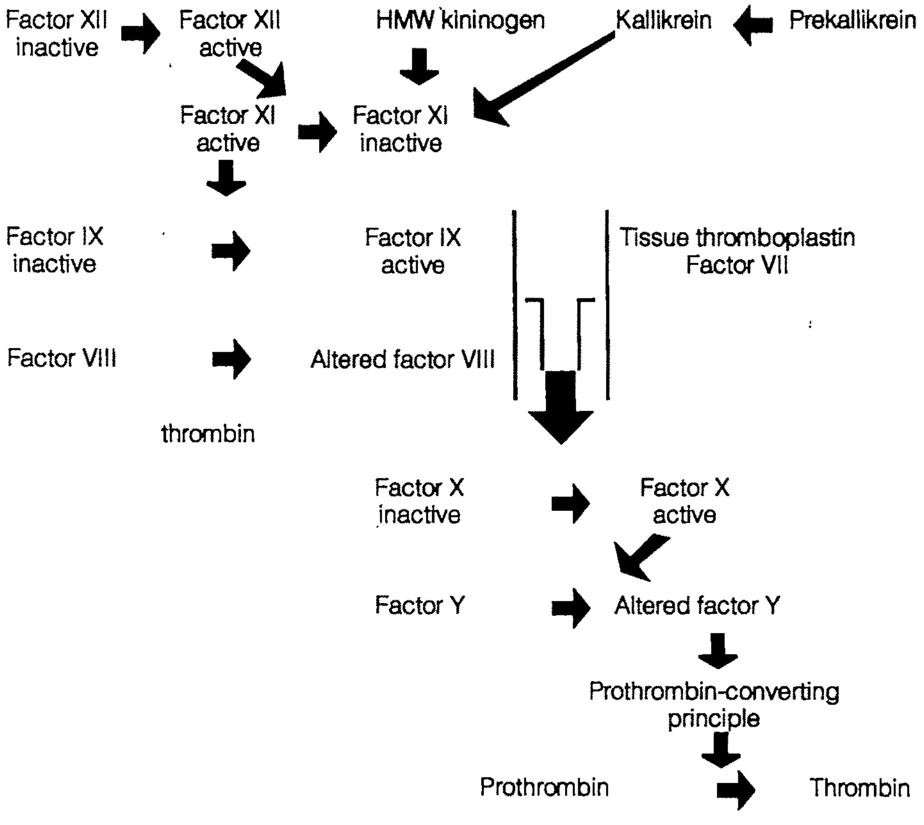

Fig. 2 The intrinsic (left) and extrinsic (right) pathways leading to thrombin formation (after Ratnoff, 1978).

of the distribution being recognised as pathological. Classic haemophilia shows clotting times outside the normal distribution and is due to a mutation affecting the gene coding for factor VIII. The clinical severity varies and this is paralleled by the quantity of factor VIII present, varying from virtually none in extreme cases to 20% of the normal level in mild cases. This might be due to a complete mutation (severe) and a leaky mutation (mild).

Christmas disease, which is indistinguishable clinically from classic haemophilia, is due to a mutation of the gene coding for factor IX. Again, the severity of the disease is paralleled by the amount of factor IX present, varying from practically nothing (complete mutation?) to a significant fraction of the normal value (leaky mutation?). Here then we have mutations of *different* genes which manifest the *same* phenotype.

Mutations of other steps in the pathway are generally less severe, either because they are leaky and the residual activity is sufficient for reasonable clotting or because defects in one pathway can be compensated by the second pathway.

Finally, the age of onset of schizophrenia must be considered. While the pathways discussed here lead to the *development* of brain function, there will be others required for its *maintenance*. Individuals who, because of mutations, have only 50% of the activity necessary for one of the steps in the pathway may not be schizophrenic unless that 50% value is altered through environmental changes. These environmental changes can be normal changes within all individuals – for example hormonal change associated with puberty – or outside the individual, for example stress of any sort. As the hormonal levels will themselves be under genetic control, they will not in all cases reach the level required to lower the 50% level posited as necessary for the onset of schizophrenia; similarly, not everyone will respond to stress in the same way.

The genetic model for schizophrenia presented here may seem complicated. However, it contains no new principles and is readily accepted by developmental geneticists to explain the development of complex biological features. This, schizophrenia surely is. We feel that the model accounts for the genetic control of the disorder better than any other available theory. What are its implications? We would list four.

Firstly, as far as genetic counselling is concerned, we do not share the optimism of those who, with that end in view, are attempting to identify *the* gene for schizophrenia. If our theory is correct, one of many different contributing genes may be responsible for the manifestation of schizophrenia in a particular family. In that case it will not be possible, for counselling purposes, to extrapolate from one family to the next. Instead, predictions would have to be based *within* families, depending on which of the many mutations leading to schizophrenia is found in the family under consideration.

Secondly, for the same reason, considerable care needs to be taken in the interpretation of twin data, on which a good deal of the theorising about the genetics of schizophrenia has depended. It follows from our model that the indiscriminate averaging of data across twin samples is meaningless: such a procedure is sensible only when the twin pairs being considered can be shown to suffer the *same* genetic mutation.

Thirdly, the contribution of the 'new genetics' to our understanding of schizophrenia is, most realistically, likely to come from the identification, cloning, and sequencing of the (perhaps many) genes that can mutate to produce the symptoms of the disorder, allowing comparison with the DNA/protein database and the possible identification of function based on sequence homology.

Finally, there is an important implication for the way we construe schizophrenia as a clinical disorder. An integral feature of our model is the *dimensionality* of the phenotypic expression due to leaky mutations and threshold effects, thus strengthening the continuity theory of psychosis developed from other evidence.

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Review Article

"Life, Jim, But Not as We Know It"?*

Transmissible Dementias and the Prion Protein

PAUL J. HARRISON and GARETH W. ROBERTS

The spongiform encephalopathies are unusual in several respects. Firstly, they are transmissible, and in some cases inheritable. Secondly, variants of these disorders occur in many species and can be transmitted by consumption of infected material; this has led to concern as to the potential risk from eating contaminated animal products. Thirdly, increasing evidence suggests that a 'prion' protein is central to their aetiology and pathogenesis, and that no nucleic acid is involved in the infective process. The role of the prion gene and its protein is outlined and proposed as the basis for an improved classification of the transmissible dementias.

The spongiform encephalopathies, or transmissible dementias, are a group of neurodegenerative disorders which in humans comprise Creutzfeldt-Jakob disease (CJD), Gerstmann-Sträussler syndrome (GSS) and kuru. Their collective name derives from the characteristic vacuolar, spongy appearance of the brain seen post-mortem. In 1959, the pathological similarities between CJD, kuru, and the sheep disease scrapie were first noted (Hadlow, 1959; Klatzo *et al*, 1959). Following these observations, essentially identical diseases (going by different names) are now recognised in many species. For 30 years these disorders have been the subject of research interest out of proportion to their apparent rarity because of a number of unique features. Most notably, each of the human forms has been shown to be transmissible by inoculation, both to other species (Gajdusek *et al*, 1966; Gibbs *et al*, 1968; Baker *et al*, 1985; Manuelidis *et al*, 1985), and iatrogenically from person to person after surgical and therapeutic procedures (Brown *et al*, 1985; Weller, 1989). Scrapie is also transmissible between animals. The crucial discovery of infectivity was followed by a search for a causative agent and an understanding of its properties, both of which remain foci of research despite significant progress in both respects.

The transmissible dementias recently achieved a higher profile with the advent of the bovine form of spongiform encephalopathy (BSE; Hope *et al*, 1989; Bradley, 1990), and the possibility that it might be transmissible to humans, as it is to mice (Barlow & Middleton, 1990), through eating contaminated beef products. Precedents for oral transmission are provided by the probable spread of kuru by cannibalism (Gajdusek, 1977) and the ability to transmit other spongiform encephalopathies by feeding infected tissue to animals, including primates (Pattison & Millson,1961; Gibbs *et al*, 1980; Kimberlin, 1990).

The occurrence of BSE and the subsequent public concern has highlighted the need to consolidate the significant strides made in the understanding of these diseases in recent years. Many of the advances have yet to reach general medical awareness, both as a result of the speed of progress, and the controversial nature of some of the key points. This review is intended to summarise these findings, emphasising their clinical significance, the underlying molecular pathology, and their relevance for the understanding and classification of neurodegenerative disorders.

The standard clinicopathological view

Creutzfeldt-Jakob disease

Since its original descriptions in 1920/21, it has become apparent that CJD has a distinctive picture (Irving *et al*, 1990), but also has variants which merge into several other conditions and which are the source of much nosological and scientific discussion.

A typical case of CJD is that of a pre-senile dementia in the absence of a family history, occurring in the sixth decade and progressing rapidly to death within a year. Women are more often affected than men (with a sex ratio of 3:2). Patients classically exhibit myoclonus and have a characteristic electroencephalogram (EEG) showing periodic triphasic discharges at 1–2 Hz. Relative to other causes of pre-senile dementia, CJD cases tend to show early visual disturbances and a variety of motor symptoms. There is no treatment able to prevent or retard development of CJD, despite occasional reports of a response to amantadine (Lishman, 1987).

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*Chief Medical Officer McCoy – Star Trek.

Creutzfeld–Jakob disease can be atypical in several ways. A familial form exists, accounting for 6–15% (Masters *et al*, 1981*a*; Will & Matthews, 1984; Brown *et al*, 1987), with a younger age of onset than sporadic cases, but longer survival. Familial cases may also be less transmissible to primates (64% of cases compared with over 90% of sporadic CJD (Brown *et al*, 1984, 1986)). CJD can take different clinical forms; for example, there are some in which ataxic symptoms are commoner, or in which muscle wasting is prominent, or which begin abruptly. These atypical forms have a variety of names and are generally thought to be exceedingly rare (e.g. Worster-Drought *et al*, 1944; Brownell & Oppenheimer, 1965; Will & Matthews, 1984).

The neuropathology of CJD is marked by the prominent spongiform appearance of the cerebral cortex, sometimes called status spongiosus (Beck & Daniel, 1987). Electron microscopy has shown this to be associated with cystic dilatation of neurones and focal necrosis of cellular membranes (Chou *et al*, 1980; Gray, 1986). Other neuronal abnormalities include swelling and loss of dendrites (Kim & Manuelidis, 1979) and axons (Gray, 1986), and accumulation of abnormal cytoskeletal protein (Nakazato *et al*, 1990). Presumably as a result of these processes, a massive neuronal loss occurs, especially in the cerebral and cerebellar cortices and striatum, whereas pathology in the hippocampus can be relatively light (Beck & Daniel, 1987). Increased numbers and activity of glia are present (Beck & Daniel, 1987; Manuelidis *et al*, 1987*a*), and white matter is also heavily affected (Bugiani *et al*, 1989). In addition, 15% of CJD brains contain extracellular amyloid plaques, usually restricted to the cerebellum (Masters *et al*, 1981*a*). Although these can be morphologically indistinguishable from the senile plaques of Alzheimer's disease (AD), immunocytochemistry has shown that they are formed from a different protein, an issue discussed below. Finally, differences in the distribution of plaques and other signs of pathology exist between CJD cases, and are counterparts of the clinical variation mentioned above.

When the triad of pre-senile dementia, myoclonus and abnormal EEG are present, clinical diagnosis is usually reliable and accurate; conversely, the absence of both the latter two features virtually excludes CJD (Brown *et al*, 1986). Unfortunately, these conditions are not always satisfied, and the occurrence of clinical variants can make definite diagnosis impossible in the absence of biopsy confirmation (Jones *et al*, 1985), neuropathology or demonstration of experimental transmissibility. To compound matters, the atypical clinical forms are less likely to show helpful EEGs (Will & Matthews, 1984). In some cases, therefore, the differential diagnosis includes all causes of dementia and ataxia. The commonest misdiagnosis is that of AD, especially for later-onset cases of CJD (about a third have an onset between 60 and 70 (Tsuji & Kuroiwa, 1983)), or the 10–25% of cases that have a course of over two years (Tsuji & Kuroiwa, 1983; Brown *et al*, 1984; Davanipour *et al*, 1988). Helpful differentiating features, apart from speed of illness progression, include cerebellar, pyramidal or extrapyramidal signs and early visual disturbances, all of which are more common in CJD (Will & Matthews, 1984; Brown *et al*, 1986). With the exception of the EEG, routine investigations are generally unhelpful in both conditions, although computerised tomography (CT) scans tend to remain normal in CJD, whereas in AD cortical atrophy is common (Galvez & Cartier, 1984; Will & Matthews, 1984).

The clinical overlap between CJD and AD is mirrored pathologically; AD can show spongiform changes (Flament-Durand & Couck, 1979; Ball, 1980; Mancardi *et al*, 1982; Smith *et al*, 1987), while CJD brains may contain Alzheimer-type senile plaques (Hirano *et al*, 1972; Brown, 1989), neurofibrillary tangles (Brown *et al*, 1990*a*), or show cell loss in the cholinergic basal nucleus (Arendt *et al*, 1984). Moreover, a third of familial AD cases are clinically indistinguishable from CJD, yet show unequivocal AD pathology and are not transmissible to animals (Brown, 1989). Other diseases which may be confused clinically with CJD include tumours, Huntington's chorea, supranuclear palsy, amyotrophic lateral sclerosis, Leigh's disease, corticostriate degeneration, and progressive multifocal leucodystrophy (Masters *et al*, 1981*b*; Brown *et al*, 1986; Irving *et al*, 1990). Most of these diagnoses are more likely to be considered if motor or bizarre neurological symptoms are prominent relative to dementia, and such cases are often seen and managed by neurologists.

Gerstmann–Sträussler syndrome

Gerstmann–Sträussler syndrome, not to be confused with Gerstmann's syndrome, is rarer than CJD, and is an autosomal dominant cerebellar disorder, in which dementia tends to be mild. Mean age at death is earlier than in CJD (around 50 years) but duration of illness is longer (4–5 years) (Masters *et al*, 1981*b*; Ridley *et al*, 1986). Most pathological features are similar to those of CJD, but amyloid plaques in the cerebellum are invariably present (Masters *et al*, 1981*b*; Roberts *et al*, 1988). Like CJD, the pathology of GSS may sometimes overlap with that of AD

(De Courten-Myers & Mandybur, 1987; Pearlman *et al*, 1988; Farlow *et al*, 1989; Ghetti *et al*, 1989; Nochlin *et al*, 1989), and the clinical and pathological pictures of GSS and CJD merge into each other (Masters *et al*, 1981*b*; Nochlin *et al*, 1989).

Kuru

Kuru is another cerebellar ataxia, associated with tremor and dementia, which runs a fulminating course leading to incapacitation and death within a year. It is notable mainly for its importance in establishing the transmissibility of the spongiform encephalopathies, and has served as a model for these diseases from which much of the subsequent research has arisen. However, it is unlikely to be encountered since it is restricted to the Fore tribe of New Guinea, and has virtually disappeared since the ending of endocannibalism there (Gajdusek, 1977).

Summary

The transmissible dementias can show an array of disease presentations and neuropathological findings, apparently overlapping not only with each other but with other neurodegenerative disorders. Until recently, there was no way unequivocally to separate one 'disease' from another, since neither clinical nor neuropathological findings are pathognomonic. However, advances from molecular biology and immunocytochemistry have provided a means for a simpler and more rational grouping of these disorders based on their underlying features. These advances also suggest that the diseases may be commoner than hitherto suspected, increasing their potential clinical significance.

New approaches from recent research

The nature of the infective agent

It is now probable that the spongiform encephalopathies occurring in various species, including the three human variants, are all caused by a single common agent. What is surprising is that increasing evidence points to the transmissible factor being a protein, called a prion (*pro*teinaceous *in*fectious agent) (Prusiner, 1982). Conversely, although not completely excluded, evidence for the involvement of DNA or RNA in the infective process – as would be axiomatic for a conventional infection of any kind – is lacking. It is the putative role of a protein as the infectious (and inheritable) cause of the transmissible dementias that would make prions a novel form of 'life' – but not as we (used to) know it (Griffin, 1985).

Prion proteins

Initial indications that the causative agent might be unusual came from several sources. Research into kuru and scrapie showed that the infectivity of affected brain tissue is not removed by procedures which are routinely used to destroy nucleic acids. Even traditional disinfectants and preservatives are often not effective – exemplified by the iatrogenic spread of CJD by intracranial EEG electrodes despite sterilisation (Weller, 1989). The agent can also pass through fine-pored filters, showing that it is much smaller than most conventional infective agents, such as viruses of the kinds that cause other neurodegenerative disorders (Matthews, 1981; Prusiner, 1982).

Infectivity could, however, be countered by proteolytic treatments, such as strong alkali or autoclaving, suggesting instead that proteins might be central to the process (Gajdusek, 1977; Prusiner, 1982). Cellular fractionation experiments have supported this view, since infectivity of different fractions generally coincides closely with the presence of the protease-resistant prion protein (PrP) (see below) (Gabizon & Prusiner, 1990). Importantly, several recent, independent techniques have also now failed to separate PrP from infectivity, or produced any evidence for the association of nucleic acid (or other non-PrP component) with infectivity (Brown *et al*, 1990*b*; Ceroni *et al*, 1990; Safar *et al*, 1990*a*,*b*).

Immunocytochemistry and immunoblotting have provided another indication of the central role of PrP in the transmissible dementias. Antibodies raised against the PrP found in scrapie-infected mouse or hamster brain cross-react with similar proteins seen in affected brains of other species, including CJD, GSS and kuru in humans (Roberts *et al*, 1986, 1988; Farquhar *et al*, 1989). This antigenic similarity is strong evidence for the unitary nature of the transmissible dementias across and within species, and emphasises the central role of this protein.

In total, a large series of experiments have produced results consistent with the hypothesis that a protein, PrP, represents the infectious agent. However, it has required additional methods to provide more compelling evidence in support of this unprecedented conclusion, and to show how the inheritability of these diseases can also be explained by the same model.

Molecular pathology of prion proteins

Making the connection between the tentative evidence that PrP might *cause* the diseases and the presence of PrP immunoreactivity as an established pathological *feature* of the transmissible dementias awaited the application of molecular biological techniques. These have determined the identity of the PrP that characterises these disorders, and allowed major advances in understanding of its aetiological role. These findings have given significant support to the 'prion hypothesis' of the spongiform encephalopathies.

The prion hypothesis came of age in the mid-1980s when it was established that PrP is encoded by a normal cellular gene (Oesch *et al*, 1985; Kretschmar *et al*, 1986*a*), located on human chromosome 20 (Sparkes *et al*, 1986). Other experiments showed that the PrP gene is expressed and its encoded protein synthesised by cells including neurones and glia throughout life (Kretschmar *et al*, 1986*b*; De Armond *et al*, 1987; McKinley *et al*, 1987; Brown, H. R., *et al*, 1990; Piccardo *et al*, 1990). These data provided unequivocal evidence that PrP production is a normal event in a healthy brain. Therefore, any pathological potential of PrP must result from an alteration in some aspect of its sequence, expression or properties. In order to distinguish the normal from the disease-associated form of PrP, they are referred to here as PrP^c (normal) and PrP^p (pathological).

Another important finding was that the prion gene in scrapie-affected animals had the same nucleotide sequence as in unaffected individuals, indicating that scrapie (at least in these cases) is not caused by a mutation (Basler *et al*, 1986). Moreover, prion gene expression is not increased during the disease (Cheseboro *et al*, 1985; Kretschmar *et al*, 1986*b*), suggesting that the deposition of PrP^p in amyloid plaques in disease is not simply the result of excessive production. Neither are variants of PrP likely to arise from differential processing of its messenger RNA, since the protein is encoded on a single exon (Basler *et al*, 1986). Further analysis of the gene sequence indicated PrP to be a 'housekeeping' gene, necessary for basic functioning of cells, in keeping with its marked conservation between organisms as diverse in evolution as fruitflies and humans (Basler *et al*, 1986). These data were also suggestive that PrP is a membrane protein, agreeing with the biochemical localisation of PrP (and infectivity) to membranes (Hunter, 1972; Meyer *et al*, 1986; Safar *et al*, 1990*a*). The cellular expression of the prion gene is summarised in Fig. 1.

These findings together answered some perplexing questions, but raised several more. The normal presence of PrP^c provided an explanation for the lack of an immune response during disease, since the

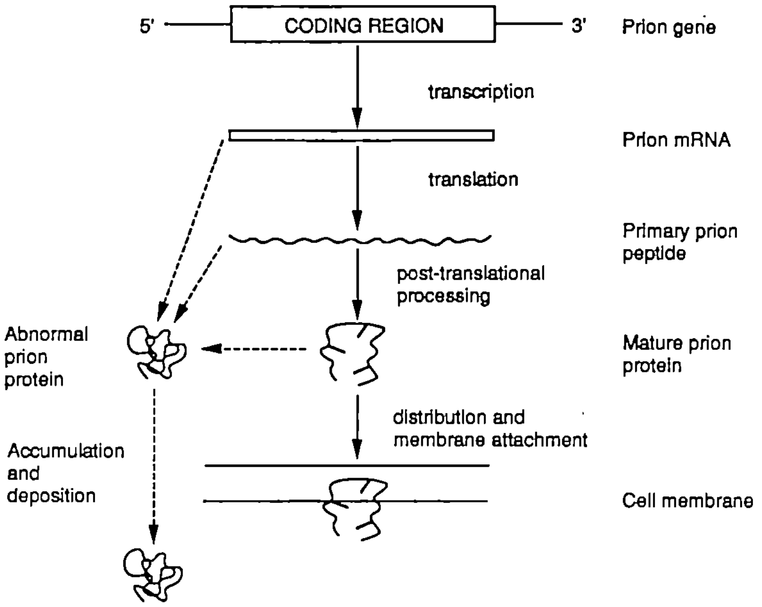

Fig. 1 Cellular expression of prion protein. The prion gene is transcribed into its complementary messenger RNA (mRNA), which migrates to the cytoplasm and serves as the template for translation into prion protein. In healthy cells, the encoded prion peptide (PrP^c) undergoes post-translational modifications before attachment to the plasma membrane (solid arrows). In infected cells, one or more steps of this process are abnormal, resulting in deposition of the protein (PrP^p) within and between cells (dashed arrows). (See also Fig. 2.)

disease-producing form of the protein is not sufficiently different to be recognised as an antigen by the host. It also removed the requirement for PrP to be a self-replicating protein to account for its proposed infectivity; its infectious properties could now be explained (much more plausibly) in terms of a disruption of pre-existing cellular PrP metabolism. Moreover, once PrP^{c} had been shown to be a normal constituent of cells, synthesised from a cellular gene, the focus could shift to a search for the abnormality which could account for its pathogenicity and differential properties in disease. For example, it provided a theoretical basis whereby cases of the human diseases might result from mutations of the prion gene, either occurring *de novo* in spontaneous cases, or incorporated in the germline in familial forms, or might be due to aberrant processing and handling of PrP itself. Subsequent genetic linkage analysis has confirmed that prion mutations do occur in some familial cases, and provides the strongest support yet for the prion hypothesis (Hardy, 1989).

Prion gene mutations

The first mutation was described by Owen *et al* (1989, 1990*a*), who found an insertion of an extra 144 base pairs at codon 52 in the prion gene in affected members of a family with CJD. Interestingly, the same insertion was then found in a case clinically diagnosed as familial AD (Collinge *et al*, 1990), and has been identified in five (out of 101) cases of atypical dementias of various diagnoses but in which CJD and GSS had not been suspected (Owen *et al*, 1990*b*). Soon afterwards, Hsaio *et al* (1989) reported a pedigree of GSS in which the prion gene contained a single base mutation, leading to an amino acid substitution (at codon 102) of proline to leucine; Doh-ura *et al* (1989) confirmed this mutation in other families with GSS, and in addition reported a new mutation at codon 189 (changing alanine to valine) in another pedigree. The link between GSS and CJD was emphasised when the same group identified the codon-102 mutation in a familial CJD case (Doh-ura *et al*, 1990); similarly, Goldgaber *et al* (1989) and Goldfarb *et al* (1990*a*) found a further mutation (at codon 200) which also occurs in both CJD and GSS cases. It is assumed, although unproven, that these mutations are the direct cause of disease in these families. It is also assumed that such mutations are pathogenic by virtue of the encoded protein having altered properties which result in cellular dysfunction and ultimately neurological disorder (see below).

Other cases of CJD and GSS probably lack these changes in gene sequence (Hsiao *et al*, 1990), although the presence of other mutations or structural alterations in the prion gene is not excluded since systematic gene analyses have yet to be carried out. As in scrapie, the presence of PrP^{p} in these cases could occur as a result of an uncharacterised gene defect or from aberrant processing of nascent PrP. Newly synthesised peptides often undergo post-translational processing and additions of various moieties before they can adopt their final conformation and position within the cell. Slight changes in any one of these steps, even when the primary amino-acid sequence specified by the gene is normal, can produce a protein with modified properties leading to alterations in its functioning and antigenicity of the type seen in the prion diseases (Gabizon & Prusiner, 1990). Indeed, the main feature that distinguishes PrP^{c} from PrP^{p} is the resistance to proteolysis of the latter; this change in property is likely to be a correlate of such post-translational modifications. For example, a specific glycolipid must be added to the carboxy-terminal of PrP to permit its attachment to the cell membrane (Stahl *et al*, 1987), while other data show that the membrane attachment and transmembrane transfer of PrP is altered in prion diseases, although the mechanisms are unclear (Lopez *et al*, 1990; Stahl *et al*, 1990; Yost *et al*, 1990). The recent identification of a PrP-binding protein homologous with a glial cytoskeletal protein which is increased in scrapie indicates additional intracellular PrP-related mechanisms requiring investigation (Oesch *et al*, 1990). More detailed molecular and cellular biology will be needed in tandem with genetic studies to establish the synthetic pathway of PrP and its abnormalities which result in deposition of PrP^{p} and production of disease.

Further support for the central role of PrP in the transmissible dementias is provided by studies investigating factors which determine the incubation period of scrapie. It has long been known that the incubation time is affected both by the strain of the host and of the infectious agent. Various theories for the basis of this phenomenon have been advanced (Hope & Kimberlin, 1987; Westaway *et al*, 1989), but it became likely from linkage data that the scrapie incubation gene was either identical to the prion gene, or very tightly linked to it (Carlson *et al*, 1986; Race *et al*, 1990). Soon afterwards, Westaway *et al* (1987) demonstrated that the two genes are almost certainly the same, by showing that mice with long incubation periods differed from those with short incubation times by variation in the prion gene sequence. Specifically, they varied in the amino acid coded for at either codon 108 or 189; the latter change was predicted to produce a significant effect on the extracellular part of PrP and its potential for post-translational modification. These differences in the host-encoded PrP demonstrate another central role for the prion gene in the disease: not only does it encode the protein associated with infectivity, it also controls the incubation period for the disease. Confirmation of these findings was given when Carlson *et al* (1989) showed that forms of the PrP encoded by these alleles indeed affected incubation time, and especially by Scott *et al* (1989), who introduced prion genes into transgenic mice and showed that different genes resulted in different incubation periods, as well as altering susceptibility to the infection and its pathological features (Lowenstein *et al*, 1990).

Together, these findings provide explanations for many aspects of these disorders for which nucleic acid in the infectious agent had been assumed to be essential (Carlson *et al*, 1989). It is now postulated that allelic heterogeneity within the prion gene, as this sequence variability is called, can explain differences in individual susceptibility to, and features of, prion-related diseases in humans (Scott *et al*, 1989). What is not clear is whether the mutations now known to be associated with cases of GSS and CJD are simply other allelic variants equivalent to those described in mice, or whether they have different relationships to the occurrence of disease. For example, the codon 200 mutation has now been discovered in some *un*affected members of the previously described pedigree (Goldfarb *et al*, 1990*b*); it remains to be seen whether these individuals subsequently develop CJD, or whether this particular mutation is not invariably associated with disease. Further study of prion gene sequences in both humans and animals is needed to clarify these points.

Mechanisms of prion pathogenicity

There is uncertainty as to the molecular events by which the inheritance of an abnormal prion gene or acquisition of abnormal PrP results in the clinical and pathological stigmata of the spongiform encephalopathies. This question is relevant whether or not prions are the sole infectious agent. A number of mechanisms have been proposed (Prusiner, 1982). If PrP^p is indeed the cause, it could produce more

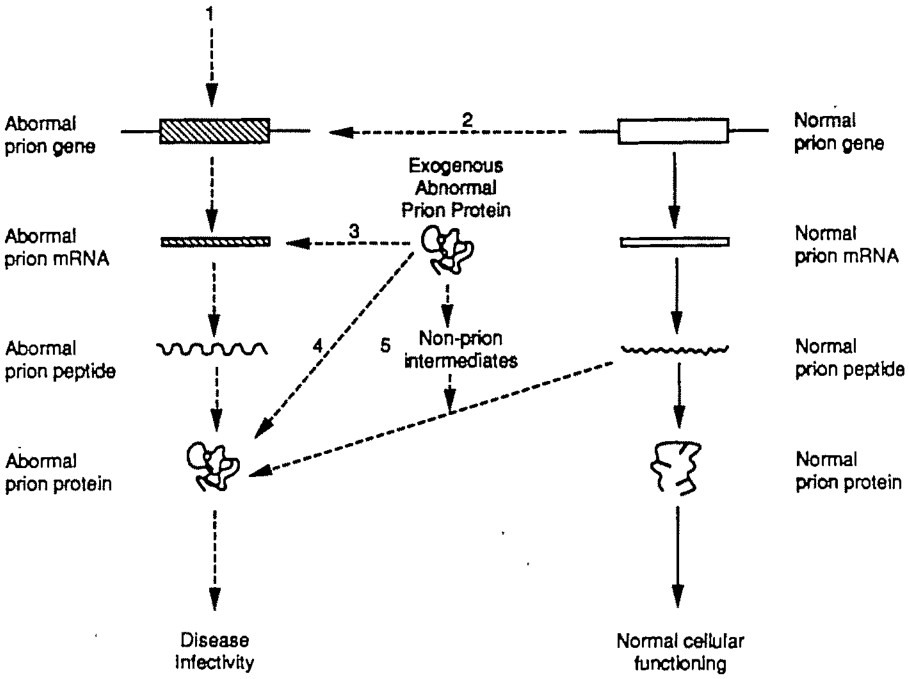

Fig. 2 Possible mechanisms for production of abnormal prions: (1) inherited abnormal prion gene; (2) spontaneous mutation of the prion gene; (3) reverse translation of abnormal prion mRNA; (4) autocatalysis of abnormal prion protein; (5) abnormal prion protein initiates its own production via non-prion intermediates. Process 1 could account for inherited cases, process 2 for sporadic cases, and processes 3–5 for cases acquired by infection. Solid arrows, normal events; dashed arrows, pathological events.

of itself either by reverse translation (whereby a protein gives rise to its encoding messenger RNA), or by promoting synthesis of further aberrant PrP molecules through a variety of indirect pathways. Some of these possibilities are shown in Fig. 2. At present, there are no data to indicate which of these candidate cellular and molecular processes actually occur to explain how the inheritance of an abnormal prion gene or contraction of infection results in production of pathology. One possibility currently under investigation to account for the acquired form is that PrP^p serves as a template for the catalytic conversion of normally produced PrP^c into more PrP^p.

Evidence against the prion hypothesis

Some workers continue to argue strongly that PrP^p is not the infective agent, although its status as a defining characteristic of the transmissible dementias is no longer in question. There are three main points against the prion hypothesis. Firstly, it remains possible that a small amount of nucleic acid (in a particle sometimes called a 'virino') could be present, intimately associated with PrP but experimentally inaccessible, by virtue of its smallness or of some unusual property. It is suggested that this putative nucleic acid co-purifies with PrP, explaining the apparent, but spurious, infectivity of PrP itself. Certainly, several resistant viruses with unexpected properties have been discovered in recent years, including the retroviruses which can become incorporated in host genomes, potentially accounting for familial forms of diseases (Ridley *et al*, 1986; Manuelidis *et al*, 1989; Sharpe *et al*, 1990). Secondly, it has been claimed that cellular fractionation experiments have, in fact, demonstrated infectivity in the absence of protein, precluding the latter as being either a necessary or sufficient infective agent (Manuelidis *et al*, 1987*b*; Czub *et al*, 1988; Aiken *et al*, 1989). The more widely accepted contrary findings of others are attributed to experimental artefacts during purification procedures (Sklavidis *et al*, 1989). Thirdly, others have shown infectivity of tissues apparently not expressing PrP (Brown *et al*, 1990), and the presence of PrP^p in tissues that are not infective (Robakis *et al*, 1986).

All these points are hotly disputed, regarding both the findings and their interpretation. It is always difficult to prove a negative, that is, that nothing but PrP^p is required to cause disease, but the weight and diversity of evidence outlined here has led to a consensus which increasingly favours the aetiological role of PrP^p. Notably, the evidence from linkage, transgenic mice and protein studies suggests strongly that expression of certain prion gene products, either through a mutation or through exogenous acquisition of abnormal PrP isoforms, is a necessary condition for the disease. This evidence markedly increases the likelihood that PrP^p is also sufficient to account for all the main features of these disorders, including transmissibility. Undoubtedly, the proponents of a more traditional aetiology based on nucleic acids will continue to provide opposing data and conclusions, which will need to be carefully considered. However, in the absence of positive evidence for a candidate nucleic acid, such interpretations are unlikely to sway the emerging consensus.

Towards a classification of prion diseases

The central and unifying role of PrP^p suggests that the transmissible dementias be renamed the 'prion diseases' to reflect this (Roberts, 1990). Whatever the roles of non-prion factors as aetiological agents, the invariant association of abnormal PrP with the spongiform encephalopathies and with transmissibility provides a basis for categorising these disorders (Roberts *et al*, 1988). Reliable detection of PrP^p by immunostaining or other methods can thereby define the diseases and be used as a diagnostic test. Within the rubric of the prion diseases, a subgrouping could be based on the origin of the PrP^p in terms of genetic (e.g. GSS, familial CJD), sporadic/idiopathic (e.g. CJD, kuru) or iatrogenic (e.g. growth-hormone-related CJD) factors, and then further classified in terms of the specific molecular causes (e.g. the exact prion mutation) as such details become apparent. This approach supersedes the inevitably inconclusive debates as to the correct nomenclature for each clinicopathological variant, or the relationship between one syndrome and another. The clinical overlap with other atypical dementias would remain a problem but could unequivocally be resolved by prion gene or protein analysis, irrespective of confounding clinical or pathological features. At present, the identification of PrP^p can only be carried out on brain tissue either at biopsy or autopsy. However, genetic analysis is rapidly becoming a diagnostic tool through regional centres, and it is hoped that improvements in immunological techniques should allow a test to be developed for demonstration of PrP^p in serum (Serban *et al*, 1990).

The value of PrP testing over conventional diagnostic approaches to possible transmissible dementias is illustrated by a recent extreme example. A familial CJD patient has been described who shared the prion gene mutation seen in other affected members of his family, yet at post-mortem examination the brain did

Table 1
A classification of the human cerebral amyloidoses

Clinical syndrome and features	Specific amyloid protein	Chromosomal location	Molecular abnormality	Nature of amyloid pathology
CJD, GSS (dementia, ataxia)	Prion	20	(a) Mutation (i) point mutations (ii) insertions (b) Abnormal protein processing?	PrP plaques
AD (dementia)	Beta-amyloid[1]	21	Abnormal protein processing?	SP, NFT?, angiopathy
Dutch amyloid angiopathy (haemorrhagic stroke)	Beta-amyloid	21	Point mutation	Angiopathy
Icelandic angiopathy (haemorrhagic stroke)	Cystatin C	9	Point mutation	Angiopathy

1. Beta-amyloid is also deposited in the brain in normal ageing, and in certain other conditions such as lipofuscinosis and arteriovenous malformations. In trisomy 21, β-amyloidosis occurs even in the absence of supervening AD, and is presumed due to increased gene dosage.
SP, senile plaques; NFT, neurofibrillary tangles.

not show significant pathology; moreover, the patient had satisfied clinical diagnostic criteria for AD (Collinge *et al*, 1990). Subsequent PrP immunostaining confirmed the presence of PrP^{p}, despite the lack of any other neuropathological features of a spongiform encephalopathy (Clinton *et al*, 1990). In this instance, therefore, conventional clinical and pathological criteria would not have correctly made the diagnosis.

Analysis of PrP may also clarify the prion positivity (and thus potential transmissibility) of other disorders, such as amyotrophic lateral sclerosis with dementia (Salazar *et al*, 1983), and other atypical dementias (e.g. Knopman *et al*, 1990; Neary *et al*, 1990), whose nosological and aetiological status is unclear. This classification of prion diseases could take its place within a broader grouping of several disorders conceptualised on similar grounds according to the nature of their cerebral amyloidosis (Table 1; Roberts *et al*, 1988); it represents an important example of the shift towards classification of neuropsychiatric disorders according to their pathogenesis, a trend which is likely to increase over the next few years, and which has general significance for psychiatry (Harrison, 1990).

Prion diseases and Alzheimer's disease – common themes

Apart from both being neurodegenerative disorders which have overlapping symptoms and pathology, prion diseases and AD are related in a number of ways, and study of each may illuminate the other.

Most importantly, the question of the transmissibility of AD has been extensively investigated. Despite occasional suggestions to the contrary (Rewcastle *et al*, 1978; Manuelidis *et al*, 1988), the overwhelming evidence is that AD is not infectious, even by intracerebral injection of affected brain tissue (Goudsmit *et al*, 1980; Brown, 1989). As discussed above, the presence of abnormal PrP appears to be synonymous with infectivity in disorders of this kind; AD, lacking PrP^{p} (Roberts *et al*, 1986), is therefore not a candidate for transmissibility.

Even if AD does not share the prion diseases' infectivity, there are still a number of interesting similarities in their pathogenesis (Gajdusek, 1985; Prusiner, 1987; Brown, 1989; Manuelidis *et al*, 1989). Both, for example, are characterised by the deposition of proteins which share the β-pleated conformation of amyloid, hence their generic name of cerebral amyloidoses. Although it is now clear that the individual proteins vary between these disorders (Table 1), they are both membrane proteins encoded by cellular genes, expressed in normal brains and other tissues, and are central to the pathological features of their associated disease. Moreover, pathology can result both from mutations of the encoding genes (Levy *et al*, 1990; Owen *et al*, 1990*b*; van Broeckhoven *et al*, 1990), and probably from abnormal processing of the gene product (see above) (Selkoe, 1989; Harrison & Pearson, 1990; Sisodia *et al*, 1990). As a consequence of either event, a change occurs in the localisation and fate of the protein, a process thought to be closely involved in producing the clinicopathological picture. Since three further groups of neurological diseases are also caused by mutations affecting amyloidogenic proteins (Palsdottir *et al*, 1988; Frangione *et al*, 1990; Mendell *et al*, 1990), it is possible that genes encoding such proteins might have a particular vulnerability to mutation (or propensity to aberrant expression); alternatively, perhaps a compensatory benefit is associated with such changes which prevents selection against these mutations (Ridley *et al*, 1986).

Cerebral dysfunction may be promoted by the loss of the normal functions of proteins with amyloid potential, as well as by the undesirable presence of the abnormal variants in an amyloid form. Although such roles are poorly understood, there is evidence, for example, that some fragments of β-amyloid are neurotrophic, while others are neurotoxic (Whitson *et al*, 1989; Yankner *et al*, 1989); changes in the differential production of these peptides in AD might affect the balance between these opposing actions. It has also been suggested that β-amyloid or its precursor acts as a receptor for a growth factor or similar ligand (Allsop *et al*, 1988). Taken together with other findings, pathogenic theories of AD involving aberrant growth and plasticity processes have therefore been formulated (e.g. Cotman & Anderson, 1988; Ihara, 1988; Barton *et al*, 1990). In this regard, it will be interesting to determine the biological actions of PrP – which are entirely unknown – since there is some evidence for the presence of similar developmental and regenerative processes in the spongiform encephalopathies (Beck, 1984; Tiller-Borcich & Ulrich, 1986; Mobley *et al*, 1988; Brown, 1989; Duguid *et al*, 1989).

Finally, neuron-to-neuron spread of disease may occur in both AD and prion diseases. For example, injection of scrapie into the eye results in a sequential appearance of pathology along visual pathways (Fraser & Dickinson, 1985). It is thought that spread occurs by slow axonal transport (in anterograde and retrograde directions) and trans-synaptic transfer (Kimberlin *et al*, 1983). Whether it is PrP itself which is distributed in this way is unknown. In AD, progression of disease along olfactory and cortico-cortical connections has been proposed (Pearson *et al*, 1985; Harrison & Pearson, 1989). The transported substance in AD is also unknown; interestingly, β-amyloid has recently been shown to undergo axonal transport (Koo *et al*, 1990). Deficiencies in neurofilament functioning have been postulated to underlie such processes in both disorders (Gajdusek, 1985).

Likelihood of accidental transmission of prion diseases

Once the fundamental similarity between animal and human types of spongiform encephalopathy is appreciated, the experimental evidence for transmissibility of these disorders within and between species leads to concern. Several points can be made. The recent spread of disease to cows, cats and dogs, and the experimental transmission of BSE to pigs, all species not previously known to be affected, could be interpreted as suggesting a modification of some property of the infectious agent, which renders humans at risk via the same process. The resistance of the agent to inactivation means that cooking of meat and culinary hygiene would not necessarily prevent this outbreak of 'food poisoning'. The long incubation period of these disorders, and the probable infectivity of affected cases before symptoms appear (Czub *et al*, 1988; Casaccia *et al*, 1989; Cathala, 1990), together enhance any risk there might be, as well as making it harder to detect until a late stage (Bradley, 1990). Finally, passage of disease through a host is accompanied by changed characteristics of the infectious agent in subsequent cases (Kimberlin, 1990); hypothetically, therefore, a bovine-modified PrP isoform could present an increased (and certainly unknown) risk to humans.

In total, therefore, several points suggest that there is some reason to be concerned about BSE. However, it is important to put this risk into perspective. For example, the extensive scrapie research is reassuring; there is no epidemiological association between the prevalence of classically diagnosed CJD and that of scrapie (Brown *et al*, 1987), nor a clear association with 'high-risk' occupations such as pathology technicians and butchers (Brown *et al*, 1987), despite anecdotal reports (Matthews, 1990) and occasional findings to the contrary (Kondo & Kuroiwa, 1982; Davanipour *et al*, 1985). The occurrence of CJD in a lifelong vegetarian may also provide comfort to meat eaters (Matthews & Will, 1981). More importantly, experimental oral transmission is calculated to be 10^9 times less efficient than intracerebral inoculation (although 1 g of infected tissue may be sufficient for oral transmission to animals) and often fails to produce disease at all (Gibbs *et al*, 1980; Prusiner *et al*, 1985). Furthermore, the apparent spread of kuru via cannibalism may in fact have been due to the agent entering through cuts and mucous membranes during ritual ceremonies with affected corpses (Gajdusek, 1977). While a similar route of infection would not preclude BSE being a health risk, it would minimise the risk still further to all except those handling animals or their carcasses on a regular basis.

The present evidence does not permit unequivocal statements that BSE and other animal equivalents are not a risk; conversely, there is no direct evidence to indicate that transmission to humans can occur (Bradley, 1990). Perhaps a reasonable position at present would be to accept that risk, albeit very small, does exist; whether or not current precautions are acceptable depends on how small is very small, coupled with an estimate of the magnitude of the consequences should the possibility become a reality.

Both epidemiological and biological data are needed to quantify this risk. Follow-up of people exposed to large amounts of BSE, such as butchers and dairy farmers, would provide indications of an increase in disease incidence. Testing for the presence of PrP^{p} and other pathological stigmata in brains of asymptomatic cows at slaughter would give a better estimate of BSE prevalence and the frequency of carriers relative to disease affected animals (Beck *et al*, 1975; Cathala, 1990).

The related question of precautions required when managing cases of human prion disease is easier to answer: CJD and GSS patients are *not* infectious and should be treated as such (Corsellis, 1979). This is in keeping with the epidemiological data, which have failed to show convincing evidence of person-to-person spread (Cousens *et al*, 1990). However, since internal organs, blood and cerebrospinal fluid all contain varying degrees of infectivity, venepuncture, lumbar puncture and surgical procedures on patients with atypical dementia should be carried out with appropriate precautions; this also applies to handling of the specimen and equipment afterwards (Gajdusek *et al*, 1977; Rosenberg *et al*, 1986). Additionally, by virtue of the proven iatrogenic spread of CJD, no patient with dementia should be a donor of any kind, in case it proves to be a transmissible form.

The potential infectivity of tissues also has implications for their handling after death. Post-mortem permission and full neuropathological investigation (including PrP immunostaining) should always be sought in order to establish diagnosis, but the possibility of a transmissible dementia should be documented and the case discussed with the pathologist. It is unfortunate that, because of exaggerated fears of the risk of infection, autopsies are rarely performed on atypical dementia cases. This is a major obstacle to pathological and epidemiological understanding of the spongiform encephalopathies, and increased efforts are called for (Corsellis, 1979). Partly as a result of the low autopsy rate, and the tendency to certify 'Alzheimer's disease' as the cause of death for any dementia lacking tissue diagnosis, the true prevalence of the prion diseases (as opposed to classic CJD and GSS) is unknown. However, it is likely to be higher than the often quoted figure of 0.5 per million (corresponding to 30 cases per year in the UK). For example, extrapolation from figures provided by a straw poll of neuropathologists gave a *theoretical* range for these disorders of 2–12% of all dementias, or 1500–9000 cases in Britain per year (Roberts, 1990). Even if the latter range overestimates the true prevalence by a factor of ten, the prion diseases would remain seriously underdiagnosed at present. Such uncertainties must be taken into account when interpreting epidemiological surveys or assessing apparent changes in disease incidence over the next few years.

Conclusions

The evidence from prion gene and protein analysis, together with anecdotal neuropathological reports, suggests that the occurrence of prion diseases (transmissible dementias), although rare, has been underestimated, and that they represent an important differential diagnosis in cases of atypical or early-onset dementia. Their clinical importance will increase further should any evidence of transmissibility from animal products emerge. Perhaps the most important advance of the past few years has been the realisation that these various disorders – both clinical variants in humans and their occurrence in different species – are fundamentally the same disease. All share the key feature of the presence of an abnormal prion protein (PrP^{p}) which can arise from mutations in the PrP gene or can be acquired infectively. Whether prions alone are a sufficient factor, although likely, has yet to be firmly established. The underlying unitary nature provided by the presence of PrP^{p} forms a basis for nomenclature, classification and diagnosis of these diseases, which is a significant advance from the traditional reliance upon clinical and pathological features.

Despite this progress, several crucial questions remain unanswered. What is the normal role of PrP^{c} and why are minor alterations in its structure so catastrophic for the brain? How can a protein be transmissible, or is an additional and elusive infectious molecule resisting discovery? Does a relationship exist between the exact PrP abnormality, the clinical picture, and the neuropathological findings in each case? What other genetic and environmental factors determine the development of these diseases? It is to be anticipated that the answers will soon emerge from a combination of molecular biology and clinicopathological research.

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Evidence for Allelic Heterogeneity in Familial Early-Onset Alzheimer's Disease

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Age of onset was examined for 139 members of 30 families affected by early-onset AD. Most (77%) of the variance of age of onset derived from differences between rather than within families. The constancy of age of onset within families was also observed in an analysis restricted to families derived from a population-based epidemiological study with complete ascertainment of early-onset AD. Furthermore, we observed clustering of age of onset within those families that support linkage to the predisposing locus on chromosome 21. Our data are compatible with the view that allelic heterogeneity at the AD locus may account for the similarity in age of onset within families. This finding may be of value for scientific studies of AD as well as for genetic counselling.

There are over 100 reported families in which Alzheimer's disease (AD) segregates as an autosomal dominant disorder (Cook *et al*, 1979; Goudsmit *et al*, 1981; Nee *et al*, 1983; Farrer *et al*, 1990). Three studies have shown genetic linkage between early-onset AD and polymorphic DNA markers on the proximal long arm of chromosome 21 (St George-Hyslop *et al*, 1987; Goate *et al*, 1989; Van Broeckhoven *et al*, 1991). Although age of onset of AD may differ considerably between families, similar ages of onset of dementia have been reported previously within several large families with apparently autosomal dominant AD (Cook *et al*, 1979; Folstein *et al*, 1988; Huff *et al*, 1988). The origin of the family resemblance in age of onset of dementia is not yet clear. The age of onset within a family may be determined by one or more genetic loci. On the other hand, given a common genetic predisposition, environmental factors shared by relatives may be involved in the onset of AD. In addition, selection bias may account for the family-specific age of onset, since relatives with similar ages of onset are more likely to be detected for genetic studies.

To investigate which factors determine the age of onset of familial AD, we examined 30 families multiply affected by AD. These families were selected for molecular linkage studies or were ascertained for an epidemiological study with complete ascertainment of patients with early-onset AD. Thus the analysis was performed in pedigrees with known linkage to a genetic locus on chromosome 21 and in a population-based unbiased sample of early-onset AD families.

Although early-onset and late-onset AD are considered as one neuropathological entity, we have excluded late-onset patients because inaccuracies in diagnosis of AD in this group may seriously bias the analysis.

Method

We studied age of onset of AD within and between 30 families derived from Belgium (Van Broeckhoven *et al*, 1991), Great Britain (Goate *et al*, 1989) and the Netherlands (Hofman *et al*, 1989) (Table 1). The families from these three studies contained totals of 62, 72 and 80 affected individuals respectively. All families had a pedigree structure consistent with an autosomal dominant inheritance of AD.

The criteria for including a family in the study were: (a) at least three individuals with clinically diagnosed AD in two or more generations; (b) detailed medical records available on the clinical diagnosis of AD of at least two affected relatives (McKhann *et al*, 1984); (c) mean age of onset below 60 years in the Belgian and British families, and (d) age of onset of the proband before the age of 60 in the Dutch study. In the Belgian and British studies, families were ascertained for genetic linkage analysis. Therefore, the mean age of onset of all affected relatives was used to select early-onset families. Different inclusion criteria were used for the Dutch epidemiological study because individual patients, not families, had been ascertained. Moreover, using the age of onset of probands to select families from this population-based study did not put any restrictions on the age of onset of the relatives. The Dutch study comprised all patients diagnosed with early-onset AD during 1980–87 in two areas of the Netherlands (Hofman *et al*, 1989); in the families of 17 patients there were at least three affected individuals known in two generations.

All molecular genetic analyses conducted with the Belgian and British pedigrees were consistent with linkage to chromosome 21 (Goate *et al*, 1989; Van Broeckhoven *et al*, 1991). Although in one British family, a cross-over between the disease locus and one of the markers

Table 1
Clinical characteristics of families multiply affected with Alzheimer's disease

Family number	Country	Mean age of onset (range): years	No. of patients	No. of pathological conformations
ADA[1]	Belgium	35 [26–45]	38	11
ADB[1]	Belgium	35 [30–39]	24	6
14	Great Britain	60 [55–65]	3	
16[1]	Great Britain	52 [45–70]	3	
23[1]	Great Britain	55 [51–62]	14	
32[1]	Great Britain	54 [47–59]	6	
34	Great Britain	44 [37–52]	3	1
53	Great Britain	52 [43–60]	5	
74[1]	Great Britain	43 [39–50]	6	2
75	Great Britain	51 [44–58]	10	
105	Great Britain	38 [36–39]	7	
121	Great Britain	37 [35–39]	4	
126	Great Britain	54 [48–63]	4	
127	Great Britain	46 [41–48]	7	
1005	Netherlands	60 [50–78]	9	
1025	Netherlands	56 [52–60]	3	
1034	Netherlands	63 [59–70]	4	
1049	Netherlands	55 [50–61]	4	1
1066	Netherlands	41 [38–49]	9	2
1068	Netherlands	55 [50–67]	4	
1070	Netherlands	59 [52–67]	4	
1072	Netherlands	60 [55–75]	6	1
1085	Netherlands	57 [50–63]	4	
1097	Netherlands	56 [48–60]	3	
1100	Netherlands	39 [35–42]	7	
1104	Netherlands	53 [47–58]	6	
1125	Netherlands	53 [49–58]	5	
1230	Netherlands	55 [49–60]	6	
1264	Netherlands	61 [56–66]	4	
1270	Netherlands	58 [47–65]	4	

[1] Families with evidence of linkage to chromosome 21 (see Goate *et al*, 1989; Van Broeckhoven *et al*, 1991).

(D21S1/S11) was inferred, there was no significant evidence for heterogeneity. Age of onset was determined through a personal interview of the next of kin of each patient, so that in each family there were multiple informants. Age of onset was estimated as the age at which memory loss or change in behaviour was first noted. This information was available for 139 (67%) of the 214 affected individuals.

Analysis of variance was used to compare age of onset among and within families (Smith, 1975). To see whether it changed over generations, the difference in age of onset was calculated for all possible combinations of sibships within a family. In the case of first-degree relatives, the difference in mean age of onset of a sibship and the age of onset of the affected parent is given. The comparison of second-degree relatives comprised the difference between the mean age of onset of a sibship and the mean age of onset of all second-degree relatives of this sibship (i.e. uncles, aunts and grandparents). In the same way, the differences were calculated between third-degree, fourth-degree, fifth-degree, sixth-degree, seventh-degree, and eighth-degree relatives.

Results

The age of onset of AD was more similar within than between families. Most (77%) of the variance in age of onset was due to differences between families (Table 2). Restriction of the analysis to the pedigrees for whom we have previously reported linkage data gave essentially similar results: 81% of variance was accounted for by between-family differences. In the Dutch data, based on complete ascertainment of patients, 67% of the variance was due to differences between families (Table 2). Unaffected siblings of these patients, however, are still at risk of AD; since ages of siblings tend to be similar, bias may occur towards a limited variation in age of onset of dementia. Upon exclusion of siblings of the probands, the intraclass correlation did not change materially (intraclass correlation 0.63, $P<0.005$).

Table 3 shows that the age of onset has remained constant in seventh-degree and eighth-degree relatives, who may have no more than 1/128 and 1/256 of their genes in common. Essentially similar results were obtained if the mean age of death of affected individuals was used. Although data on environmental toxins were not available, we compared ages of onset of relatives raised apart to see whether there was evidence for a modifying role of environmental factors. The average difference in age of onset between sibships of

Table 2
Analysis of variance between and within families multiply affected with early-onset Alzheimer's disease

Families	Source of variation	Degrees of freedom	Mean sum of squares	*P* value	Intraclass correlation
All families	Between	29	407.20	0.0005	0.77
	Within	109	24.46		
Families with evidence of linkage to chromosome 21	Between	5	663.04	0.0005	0.81
	Within	39	22.20		
Population-based families	Between	15	184.91	0.0005	0.67
	Within	42	25.11		

Table 3
Difference (s.d.) in age of onset between sibships by degree of relationship

Degree of relationship (genetic distance)	Belgian families	Dutch families	British families	All families	Families with reported linkage to chromosome 21
First	6.0 (4.4)	4.8 (3.3)	5.9 (5.8)	5.3 (4.5)	5.4 (3.2)
1/2	($n=3$)	($n=19$)	($n=14$)	($n=36$)	($n=7$)
Second	4.0 (3.2)	7.6 (3.0)	3.8 (3.6)	4.9 (3.7)	4.3 (3.5)
1/4	($n=7$)	($n=10$)	($n=18$)	($n=35$)	($n=12$)
Third	5.5 (2.8)	5.0 -	3.0 (2.3)	4.1 (2.7)	5.1 (2.7)
1/8	($n=10$)	($n=1$)	($n=14$)	($n=25$)	($n=12$)
Fourth	4.2 (2.7)	-	1.7 (2.9)	3.5 (2.9)	4.2 (2.7)
1/16	($n=8$)		($n=3$)	($n=11$)	($n=8$)
Fifth	3.3 (2.3)	-	-	3.3 (2.3)	3.3 (2.3)
1/32	($n=8$)			($n=8$)	($n=8$)
Sixth	4.7 (3.8)	-	-	4.7 (3.8)	4.7 (3.8)
1/64	($n=12$)			($n=12$)	($n=12$)
Seventh	4.7 (3.2)	-	-	4.7 (3.2)	4.7 (3.2)
1/128	($n=10$)			($n=10$)	($n=10$)
Eighth	3.3 (2.7)	-	-	3.3 (2.7)	3.3 (2.7)
1/256	($n=8$)			($n=8$)	($n=8$)

a family born more than 50 km apart (3.7 years, s.d. = 3.0, $n = 13$) was similar to the difference found for sibships born less than 50 km apart (4.4 years, s.d. = 3.0, $n = 54$).

Discussion

These data show that age of onset of AD is more similar within multiply-affected families than between families. The analysis of the population-based data indicates that this finding is not due to ascertainment bias. Determination of age of onset may still be subject to error. Collecting data through interviews of relatives may have led to artefactual clustering of age of onset within families. However, it was always obtained from a family history from the next of kin of each patient, that is, there were multiple informants within a family. Since in the large pedigrees, ages of onset were obtained from informants who did not know of the relationship to other patients in the pedigree, this information can be considered as independent. The finding that the age of onset remained constant even in eighth-degree relatives strongly supports the existence of a family-specific age of onset. Moreover, an analysis of age of death, dates of which were always checked against independent medical records, demonstrated the same effect.

In accordance with other studies of onset of dementia in relatives raised apart, our findings do not support a strong influence of environmental factors. A constant age of onset has been reported within a large Italian pedigree, although relatives lived as far apart as France, Italy and the USA (Foncin *et al*, 1986). Similarity in environmental factors and lifestyle are likely to decrease if members of a family are more distantly related. Age of onset, however, did not differ significantly with distance in relationship or place of birth in our analysis. Although environmental neurotoxins (e.g. aluminium) may play a role in the aetiology of AD, our results show that within early-onset pedigrees there is little evidence of a predominant influence on age of onset.

The data from families which support linkage to chromosome 21 suggest that the characteristic age of onset of a family may have a genetic origin. There are two possible explanations for this: (a) other genes, which are coinherited with the locus on chromosome 21, may modify the age of onset; (b) different alleles at the same genetic locus predispose to different ages of onset, that is, there is allelic-heterogeneity. The first explanation would predict that within a family recombination between the AD locus and the putative onset-determining locus may occur. Thus the variation in age of onset would increase when family members are more distantly related. Since age of onset appears to be constant within a family through different generations this explanation is less likely. Although the molecular genetic analyses were consistent with linkage to chromosome 21 in all families, significant linkage data were not obtained in each family. Therefore, we cannot exclude the possibility of non-allelic genetic heterogeneity with some families. However, the specific age of onset AD observed in the analysis of families with evidence of linkage to the predisposing locus on chromosome 21 suggests that there may be different mutations at the same locus (allelic heterogeneity).

There are several implications of our findings. Firstly, it may be possible to detect those individuals who fall outside of the expected age of onset for a particular pedigree. Patients detected in this way may represent non-genetic forms of AD, probably representing the population risk. In genetic studies, it may be of great value to distinguish these patients. Studies of these 'non-genetic' patients may also reveal the role of neurotoxins (e.g. aluminium) and environmental risk factors in AD. Secondly, these findings have relevance for genetic counsellors in assessing the risk to an individual of having inherited the predisposition to the disease. Thirdly, if allelic heterogeneity does exist between pedigrees, then it will not be possible to use linkage disequilibrium to map the genetic defect.

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Social Deprivation and Rates of Treated Mental Disorder

Developing Statistical Models to Predict Psychiatric Service Utilisation

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A review of the literature shows that there are strong associations of treated prevalence rates of psychiatric disorder with social class, sex, marital status, ethnic group and living alone; and moderate associations with living in inner-city areas and a high degree of residential mobility. The Jarman-8 index of social deprivation correlates with psychiatric admission rates for patients aged less than 65 years (R^2=0.38). Individual census variables can themselves account for up to 0.71 of the variance in the admission rates, while combined in a stepwise multiple regression the census variables will account for over 0.95 of this variation. Multiple regression models using individual census variables and derived indices should be applied next on a wider geographical basis, and to narrower age, sex and diagnosis-specific psychiatric morbidity rates.

This paper has three aims: firstly, to identify from the literature which sociodemographic factors have clearly identified associations with psychiatric morbidity rates; secondly, to replicate for the South East Thames Region (SETRHA) the North West Thames study (Hirsch, 1988), which found high correlations between the district Jarman-8 scores and the total adult admission rates, and the under 65 admission rates ($r=0.76$ and $r=0.80$ respectively); and thirdly, to test a series of multiple regression models for their ability to statistically account for the variation between health districts in psychiatric admission rates.

Five hypotheses will be examined in this study: (a) that the correlation between district psychiatric admission rates (adults under 65 years) for the SETRHA will correlate significantly with the district Jarman-8 indices; (b) that the Jarman-8 index will better predict district admission rates than do Standardised Mortality Ratios (SMRs), the ACORN index (1986), the Unit9 and the Department of the Environment (DoE) Social Indices (see below); (c) that the Jarman-8 index will better predict district admission rates than do single sociodemographic variables; (d) that single census variables combined in a multiple-regression model will account for a greater proportion of the variance in SETRHA district admission rates than do any single census variable or derived index; and (e) that a principal components analysis will identify meaningful components which will predict admission rates better than single census variables, single derived indices, or combined census variables.

Sociodemographic variables and psychiatric disorders

In 1939 Faris & Dunham described a clear gradient of psychiatric admission rates for psychosis in Chicago, with higher rates in the inner-city areas. More recent work at the ecological level has focused on treated prevalence in relation to four issues: intra-urban patterns, urban–rural differences, the effect of geographical distance from services, and the association with population density.

With regard to intra-urban patterns Hare (1956) reported a strong association in electoral wards between admission rates for schizophrenia and the proportion of people living alone. He concluded that the data supported two possible explanations: that social isolation is a causal factor for schizophrenic episodes or that schizophrenic people segregate in these areas. Such patterns may be very stable: they were found to persist in Bristol 20 years later but were then in areas with high proportions of first- and second-generation Afro-Caribbeans (Harrison *et al*, 1984; Ineichen *et al*, 1984). Similar patterns have been demonstrated in Nottingham (Giggs & Cooper, 1987) and in Mannheim where between 1965 and 1980, despite marked local sociodemographic changes, the spatial distribution of incident cases of mental disorders showed a correlation of $r=0.73$ over the 15-year study (Weyerer & Haefner, 1989).

While rates of treated mental disorder have been shown to be higher in urban than in rural areas (Eaton, 1974; Goodman *et al*, 1983), these data have not adequately accounted for the effects of migration, for the presumed stresses of urban life and for service availability (Eaton, 1974). Reviewing this literature, Dohrenwend (1975) showed that overall prevalence rates of psychosis showed little rural-urban difference, but that schizophrenic rates appeared higher in cities and rates of manic-depressive psychosis lower. There was also evidence in favour of higher urban rates of neurosis and personality disorder.

In addition, the effects of age and social class may differ between urban and rural areas. Using the Maryland Psychiatric Case Register, Eaton (1974) found that hospital admissions for schizophrenia occurred later in rural areas, a result later confirmed in Ireland by Keatinge (1989), although again limited by reliance on treated rather than true prevalence rates (Cagle & Banks, 1986).

Goldberg & Huxley (1980) have demonstrated that selection and referral filters modulate and direct recognised psychiatric morbidity from the primary to the secondary and tertiary care sectors. The extent to which service utilisation is related to service availability is much less well documented. Considering here only geographical availability, a model developed in Auckland showed that distance from health centres was a significant predictor for utilisation rates in three psychiatric intervention services (Hall, 1988). Even so, the reduction in demand with distance appears to be non-linear (Srole, 1975), as a study in western Australia has illustrated (Stampfer *et al*, 1984).

Data examining the contribution of population density to psychiatric morbidity is sparse. In his Bristol study Hare (1956) found a correlation of 0.37 with admission rates for schizophrenia, and −0.39 for the neurotic disorders. A larger study of 13 parliamentary constituencies in London and six electoral wards in Sheffield (Lomas *et al*, 1973) found a range in population density from less than eight to over 60 persons per acre, and a highly significant correlation with the schizophrenia discharge rate of 0.83.

Associations with derived sociodemographic variables

Social class and social security benefits are two derived variables whose association with psychiatric morbidity has been examined. The association between social class and mental disorder is best documented and established for schizophrenia (Hollingshead & Redlich, 1958; Goldberg & Morrison, 1963; Dunham, 1965; Eaton, 1974; Kohn, 1976; Eaton, 1985; Jablensky, 1986, 1988; Shur, 1988; Wyatt, 1988). Reviews of both true prevalence (Dohrenwend & Dohrenwend, 1969) and of treated incidence (Eaton, 1974) have shown that low social class confers a relative risk of 2–3 for schizophrenia. Social status has most often been defined in the USA by using education or income (Kessler, 1982; Liberatos *et al*, 1988) and in Britain by the Registrar General's classification (Goldberg & Morrison, 1963).

For schizophrenia, lower social class is associated with longer duration of episode (Cooper, 1961), greater risk of relapse (Myers & Bean, 1968), poorer quality of care (Mollica & Milic, 1986*a*,*b*), lower per capita treatment expenditure (Hollingshead & Redlich, 1958) and poorer treatment response and clinical outcome (Cooper, 1961; Weyerer *et al*, 1982). It is also associated with disproportionate utilisation of psychiatric services (Lavik, 1983) and with differing perceptions of mental illness (Heller *et al*, 1979). Further, a study in Bavaria has suggested that the effect of social class on prognosis may diminish with increasing length of stay (Weyerer *et al*, 1982).

Explanations of these findings use two models: social causation and social selection/drift. The social causation model suggests that exposure to social, especially urban, stressors induces onset or relapse of schizophrenia (Link *et al*, 1986). The selection/drift model proposes two processes which jointly produce downward social mobility. Firstly, there is intergenerational mobility which involves a reduction in social status in relation to the parental generation. Secondly, intragenerational 'drift' occurs, which is a progressive deterioration in the patient's own relative socioeconomic standing (Turner & Wagenfield, 1967; Eaton, 1980, 1985; Wiersma *et al*, 1983).

With regard to social security benefits, British data on the receipt of severe disability allowance, invalidity benefit, sickness benefit and attendance allowance, although classified by ICD category for cause of disability, are not available for any smaller unit than the 11 standard statistical areas of Great Britain, and so are of little use in predictive models. Their potential, however, has been demonstrated in the USA. Goldman *et al* (1981) attempted to formulate an operational definition of severe mental disorder along the three axes of diagnosis, disability and duration. The uptake levels of Supplemental Security Income (SSI) was used as a proxy for combined severity of disability and duration (greater than 12 months), and allowed an estimate of between 1.7 and 2.4 million people who suffer from severe mental disorders in the USA. This estimation method, used in Oslo, indicated that patients receiving disability pensions were relatively more frequent and more intensive users of the local psychiatric services (Lavik, 1983).

A variation employed by Shapiro *et al* (1985) using Epidemiologic Catchment Area (ECA) data is to define poverty by the proportion of the population registered for the state health insurance, Medicaid. Using such a scheme, they describe a strong gradient of greater psychiatric needs, and lower levels of met need among Medicaid recipients.

Associations with individual sociodemographic variables

Treated prevalence rates of the neurotic disorders are higher among women, and personality disorders more prevalent among men (Dohrenwend, 1975). Data from the ECA multisite survey in the USA demonstrated that, for all diagnoses, a higher proportion of women made mental health visits, but that men in contact with services were more likely to be seen by a mental health specialist (Shapiro *et al*, 1984). For schizophrenia, treated prevalence rates for men are higher (Eaton, 1985; Sartorius & Jablensky, 1986; Jablensky, 1988), onset is earlier, and course, outcome and treatment response are poorer (Wyatt *et al*, 1988). Furthermore, men's premorbid social functioning is poorer (Eaton, 1985), and they make greater demands upon services for the long-term mentally ill (Hughes, 1973; Lavik, 1983; Liberatos *et al*, 1988).

In his review, Warr (1987) indicates that unemployment may impair physical and mental health (especially anxiety and non-psychotic depression), and increase smoking, suicide and deliberate self-harm. Analyses of aggregate data are as yet less conclusive, although divorce rates appear to increase. Further substantiating these links, analyses carried out in Sheffield and Hackney found a correlation between admission rates for schizophrenia and unemployment levels of 0.87 (Lomas *et al*, 1973).

Drawing on eight previous studies, Eaton (1985) calculated a mean relative risk of schizophrenia of 3.0–4.7 for non-married compared with married individuals. The widowed have a lesser risk than the divorced, separated and never-married (Eaton, 1975), while heavy service users are more likely to be unmarried (Lavik, 1983). Indeed, in one Connecticut study the association between marital status and relative risk had remained relatively unchanged over 25 years (Mollica & Milic, 1986*b*).

Living alone, living in overcrowded accommodation and living in council housing are all related to higher psychiatric prevalence rates. In the ECA study, people living alone had very high rates of need, of which a high proportion was unmet (Shapiro *et al*, 1985). Overcrowding was used in the predictive model of Lomas *et al* (1973) who found a correlation of 0.90 between the percentage of the population living at more than 1.5 persons per room and schizophrenia discharge rates.

From the early work of Faris & Dunham in Chicago (1939) emerged the suggestion that residential mobility is associated with rates of mental disorder. That schizophrenia rates are higher in the inner-city 'zones of transition', characterised by a highly itinerant population, has been reinforced more recently by work in Los Angeles (Dear & Wolch, 1987).

There is now substantial evidence that patients' ethnic group may have a profound influence upon psychiatric morbidity rates (London, 1986). Most large studies report treated morbidity and suggest that both schizophrenia and all-diagnosis rates for West Indian and Irish patients, for example, are at least twice those of white English patients (Hemsi, 1967; Cochrane, 1977; Rweglera, 1977; Carpenter & Brockington, 1980; Littlewood & Lipsedge, 1981; Dean, 1981; Cochrane & Bal, 1989; Glover, 1989). Indeed, a more recent study in Nottingham, using standardised instruments, found that utilisation rates may be even higher among second-generation Afro-Caribbeans (Harrison, 1987).

Mediators between census variables and service use

The sociodemographic factors referred to above have most often been directly correlated with various psychiatric morbidity indices, most often in-patient admission rates. Several authors, however, have attempted to go beyond this descriptive level and interpret the results in terms of three constructs presumed to mediate the relationships: poverty, social isolation and social disorganisation (Department of Health and Social Security, 1980).

Using health indicators, a study in Bristol concluded that poor health is significantly correlated with material deprivation (Townsend *et al*, 1985). In relation to psychiatric morbidity, an analysis of electoral ward data in Edinburgh and Glasgow found correlation coefficients of 0.45 to 0.53 between a combined index of deprivation and psychiatric admission rates (Carstairs, 1981). Total household income would arguably be the best index of material deprivation, but, like social security benefit data, is not available for small-area comparisons.

Social isolation as a mediator between sociodemographic characteristics and psychiatric morbidity was proposed by Hare (1956). From his findings in Bristol, that schizophrenia admission rates correlated with districts with a high proportion of the population living alone, he concluded that this was consistent either with social isolation acting as causal factor in incident cases, or with the segregation hypothesis that affected individuals clustered in poorer, isolated households. The finding was replicated in a community mental health survey of New Haven, Connecticut (Tischler *et al*, 1975). Patients who were unmarried, unemployed, living alone or without religious affiliations were disproportionately heavy users of the mental health services.

A disintegration of social functioning has been associated with high psychiatric morbidity rates since the earliest Chicago studies. Disorganisation has been characterised by excessive residential mobility, ethnic conflict, communication breakdown, and a lack of consensus (Dunham, 1965). Although conceptually interesting, there is little empirical evidence for this view (Bebbington & Davies, 1980; Weyerer & Haefner, 1989).

Psychiatric morbidity and service use

Psychiatric morbidity data based upon service-contact rates show a highly biased picture that may grossly underestimate true incidence and prevalence rates, and which may distort or even reverse aetiological associations.

Reviewing 13 epidemiological studies, Link & Dohrenwend (1980) estimated that for all psychiatric diagnoses the median proportion of (true) cases in treatment was 27%, with considerable variations between diagnostic groups. Overall, more serious conditions are more likely to have been in treatment. For all psychoses the proportion treated is 60%, and for schizophrenia 83%. Consistent with this, the ECA study determined that a majority of psychiatric cases ascertained by the Diagnostic Interview Schedule had not seen a mental health provider during the previous six months, and that the proportions were especially low among those with cognitive disorders, and alcohol and drug abuse (Shapiro *et al*, 1984).

Sociodemographic factors in turn mediate the referral process that brings true cases into service contact. There are higher proportions of treated cases among young adults, men, city dwellers, and in those who are divorced or separated. While true rates are inversely related to social class, treated rates are directly associated with this variable (Link & Dohrenwend, 1980). In the ECA study, psychiatric needs were less often met for those who were elderly, living alone, or receiving Medicaid (Tischler *et al*, 1975; Shapiro *et al*, 1985).

Statistical models to predict service use

The literature reviewed in the previous sections indicates that many social and demographic variables are individually and jointly associated with rates of psychiatric service usage. Firstly, there is strong evidence to relate such rates with social class, sex, marital status, ethnic group, and living situation. Reasonable evidence links utilisation rates with living in inner-city areas, and a high degree of residential mobility. The evidence is less firm in implicating geographical distance from services, population density and the levels of social security received as possible predictor variables. Secondly, it is clear that many of these sociodemographic variables are highly inter-related (the statistical problem of multicolinearity). Thirdly, there appear to be interactions between utilisation and age, sex, social class, marital status, and place of residence. We therefore developed statistical models to further explore the relationship between sociodemographic variables and service use in the South East Thames Region.

Method

The South East Thames Regional Health Authority (SETRHA) provides a service to the 3.6 million people living to the south and east of London as far as the Sussex and Kent coasts. The inner-city areas of London have experienced an outflow of population over the last ten years. The region has one of the highest proportions of elderly in England – a proportion that continues to increase. The overall social class distribution is similar to that of the whole nation. Regional psychiatric services, in line with national policy, are being decentralised (SETRHA, 1989; Thornicroft & Bebbington, 1989). Nevertheless, in 1986 84% of all psychiatric beds were still sited in the seven large institutions, while seven of the 15 districts have no in-patient psychiatric facilities on their district general hospital sites. In terms of treated psychiatric morbidity, it has higher than national average rates of admissions, patient turnover and residents in psychiatric hospitals (Department of Health and Social Security, 1984, 1985).

Procedure

The analyses use three types of variables: individual census variables (predictor variables), derived indices of social deprivation (also predictor variables), and psychiatric admission rates (outcome variables). The predictor variables used are from the 1981 census Small-Area Statistics (OPCS, 1981), from SETRHA (Rice *et al*, 1984), and from Professor Jarman.

Outcome data were derived from the SETRHA annual reports of the Mental Health Enquiry (MHE). Regional admission data were made available by the Department of Health as the national MHE tape for 1982, and Professor Jarman provided admission rates for the SETRHA districts standardised by age, sex and marital status. The analyses presented here concern the crude and standardised admission rates for adult patients aged less than 65 years for the district health authority of residence, not treatment.

MHE data are only available for health districts after the 1982 reorganisation, and for this reason 1981 census data are correlated with 1982 MHE data, and there may be a minor degree of slippage over the elapsed year. The reliability of the census data was tested by cross-reference between the three data sources. The outcome variables were taken from standard regional MHE tables whose validity is checked by the Department of Health in comparison with daily ward returns.

Table 1 summarises the components of four of the derived indices of social deprivation used in the analysis. Jarman has produced a composite index of social deprivation (Jarman, 1983, 1984), aiming to identify areas in Britain which are relatively underprivileged (Department of Health and Social Security, 1976; Bebbington & Davies, 1980; Townsend *et al*, 1985). There are two versions based upon eight and ten census variables (Jarman-8 and Jarman-10) which are weighted in accordance with the judgments of a national survey of general practitioners on the factors which increase workload, standardised and transformed. The Jarman-8 score has become the more widely used.

Despite criticism of this approach (Scott-Samuel, 1984; Wilkin *et al*, 1984; Bickler, 1988; Carr-Hill, 1988), it has gained external criterion validity (Charlton & Lakhani, 1985) and has become widely recognised as a useful summary measure of social deprivation (Leavey & Wood, 1985).

The Unit9 index (Department of the Environment, 1983) is calculated from nine census variables which are given equal weighting. The variables are those used in the Jarman-8 without the change of address item and adding scores for lack of amenities and the population aged over 65 years. The DoE Social Index also uses eight census variables, with weights of 1 or 2 (Department of the Environment, 1983; Irving & Rice, 1984). In addition, the standardised mortality ratio (SMR) (OPCS, 1986) for all age groups and for those aged less than 65 (SMR65) were used as predictor variables.

A further index of social deprivation used, the ACORN index (A Classification of Residential Neighbourhoods), also draws on variables from the 1981 census. Enumeration districts are categorised using cluster analysis into 38 different types on the basis of 40 census variables measuring age, housing conditions, and socioeconomic status (ACORN, 1986). Individuals may be linked via their enumeration district to an ACORN type by using the address postcode. Account can be taken of the influence of supply of services on utilisation, and the analysis here will employ ACORN ratings both with (ACORNS) and without (ACORNN) this supply correction.

Table 1
Calculation of derived sociodemographic measures by weighting census scores: weights used

Census variable[1]	Jarman-8	Jarman-10	Unit9	Social Index
Over 56	0	6.19	1	0
Elderly alone	6.62	6.62	1	2
Children under 5	4.64	4.64	1	2
One parent	3.01	3.01	1	2
Unskilled	3.74	3.74	1	0
Unemployed	3.34	3.34	1	2
Lacks amenity	0	3.60	1	1
Overcrowded	2.88	2.88	1	1
Changed address	2.68	2.68	0	0
Ethnic minority	2.50	2.50	1	1

1. See Appendix for full definition of variables.

Results

Model 1: correlations of admission rates with individual census predictor variables

The correlations between individual census variables and the outcome variables are given set out in Table 2, and definitions of the census variables used are shown in the Appendix. Table 2 demonstrates that, with the exception of the age-specific predictor variables, all the census variables are strongly or very strongly correlated with the outcome variables.

Table 2 also shows the R^2 value, that is the proportion of variance (R^2) of each outcome variable which is explained by each individual predictor variable. The census variables which account for the highest proportion of the variance in the crude admission rate are, in rank order, overcrowding (over 1.5 people per room), lack of household amenities, living in one room, change of address in last year, overcrowding (over one person per room), population density, ethnic composition, no access to a car, and being a single parent.

Model 2: correlations with derived predictor variables

The derived census variables were separately inserted into the linear regression procedure, and the results are displayed in Table 3. The three derived variables most successfully predicting the unstandardised admission rate are, in rank

Table 2
Correlations between outcome variables and individual census variables

Census variable[1]	Correlation with: Crude admission rate		Standardised admission rate	
	R	R^2	R	R^2
Elderly alone	0.12	0.01	−0.03	0.0009
Children under 5	0.12	0.01	−0.03	0.0001
Single parent	0.65	0.42	0.59	0.34
Social class V	0.50	0.25	0.52	0.27
Unemployed	0.57	0.33	0.52	0.27
Lack of amenities	0.83	0.69	0.75	0.56
Overcrowded 1	0.71	0.50	0.68	0.46
Overcrowded 2	0.84	0.71	0.79	0.62
Changed residence	0.71	0.51	0.59	0.35
Ethnic minority	0.67	0.45	0.63	0.40
No car	0.66	0.40	0.59	0.35
Living in one room	0.77	0.59	0.66	0.43
Population density	0.68	0.46	0.66	0.43
General beds	0.65	0.42	0.60	0.36
Psychiatric beds	0.30	0.09	0.29	0.08
Nursing home beds	−0.18	0.03	−0.26	0.07

1. See Appendix for full definition of variables.

Table 3
Regression of derived variables by outcome variables

Derived variable	Correlation with:			
	Crude admission rate		Standardised admission rate	
	R	R^2	R	R^2
Jarman-8	0.62	0.38	0.54	0.30
Jarman-10	0.56	0.31	0.45	0.20
SMR	0.32	0.11	0.37	0.14
SMR65	0.52	0.27	0.46	0.21
ACORNN[1]	0.52	0.28	0.52	0.27
ACORNS[1]	0.53	0.28	0.53	0.28
Unit9	0.63	0.40	0.55	0.31
Social index	0.65	0.42	0.56	0.32

1. Ratings with (ACORNN) and without (ACORNS) correction for the influence of supply of services on utilisation.

order, social index, Unit9, and Jarman-8. It is notable that they each account for just over a third of the outcome variance, compared with just over two-thirds by the better individual census variables.

For the standardised outcome rate, the same derived variables in the same rank order, best predict admissions. Again, the extent of the prediction is slightly less for the standardised than the unstandardised rates. This was expected as the variability of the admission rates due to age, sex and marital status has been removed by standardisation.

Model 3: stepwise multiple regression with individual census variables

The forwards-stepwise form of multiple regression analysis first adds the single predictor with the highest contribution to the variance of the outcome variable, and then in turn adds further predictor variables one at a time as long as each new addition produces a significant improvement in the R^2 value. It should be noted that the order and relative contributions of the predictor variables in this approach are relatively unstable, and the output cannot be considered as the 'best' model.

For the crude admission rates, the two predictors which added significantly to the model (with the cumulative R^2 values) were overcrowded 2 (0.71) and ethnic minority (0.83). Seven other factors, which brought the combined R^2 to 0.95, were population density, overcrowded 1, social class V, availability of general beds, living in one room, nursing home places available, and availability of psychiatric beds. For the standardised rates, the significant predictors were overcrowded 2 (0.62) and single parent (0.74), while another seven variables brought the R^2 to 0.93: general bed availability, unemployment, living in one room, population density, overcrowded 1, children under aged five years, and changed accommodation (see Appendix for explanation of variables).

Model 4: principal components analysis

The principal components analysis (PCA; Armitage & Berry, 1989) was performed for all census variables and produced three interpretable components (Prin1, Prin2, Prin3; Table 4). The advantage of PCA is that it allows census variables to be identified from within each component which are both relatively independent, and which together contribute towards a high R^2 value in a multiple regression model.

The first three components together account for 92% of the variance within predictor variables entered into the model. The first component has only moderate loadings from a wide range of census and population factors, and represents a general deprivation factor ($R^2=0.59$). The second component has highest loadings for the variables elderly living alone, living alone, and those registered as permanently sick, and represents the socially isolated who are physically infirm and who use psychiatric services ($R^2=0.26$). The third component is primarily loaded by the availability of psychiatric services, the lesser loadings suggesting that this element of psychiatric bed usage is particularly taken up by those young adults who are unemployed, in social class V, and socially isolated ($R^2=0.07$).

Model 5: multiple regression model of components 1–3 by crude admission rate

The components identified in the PCA were inserted serially into a multiple regression model for both the crude and standardised admission rates. The three principal components together account for about two-thirds of the variance of the outcome variables. For the crude admission rates, the cumulative R^2 values from adding the three principal components were 0.50, 0.54 and 0.68, while the corresponding values for the standardised admission rates were 0.44, 0.45 and 0.58.

Table 4
Principal components analysis: loadings of census variables to components Prin1–3

Variable[1]	Prin1	Prin2	Prin3
Elderly alone	0.02	0.43	−0.17
Single parent	0.29	−0.01	−0.07
Social class V	0.26	−0.13	−0.21
Unemployed	0.26	0.02	−0.31
Changed residence	0.25	0.20	−0.02
Ethnic minority	0.28	−0.07	0.07
Lack of amenities 1	0.24	0.12	0.30
Overcrowded 1	0.28	−0.09	−0.01
Living alone	0.19	0.32	−0.02
No car	0.28	0.07	−0.17
Permanently sick	−0.13	0.37	−0.19
Living in one room	0.23	0.21	0.16
Population density	0.27	−0.09	0.07
General beds	0.25	0.08	0.06
Psychiatric beds	0.02	−0.18	0.77
Nursing home beds	−0.11	0.37	0.10

1. See Appendix for full definition of variables.

Table 5
Summary chart of complexity and predictive power of models used

Model	Model type	Number of variables	R^2 crude	R^2 standardised
1	Regression with census variables	1	0.71	0.62
2	Regression with derived variables	1		
		Jarman-8	0.38	0.30
		Unit9	0.40	0.31
3	Stepwise multiple regression	3	0.86	0.77
		5	0.90	0.82
		9	0.95	0.93
5	Principal components analysis	1	0.50	0.44
		2	0.54	0.45
		3	0.68	0.58
6	Multiple regression with variables identified in model 5	3	0.80	0.69
		4	0.84	0.74

Model 6: multiple regression model using variables identified by principal components analysis

Model 6 uses three census variables, one taken from each of the principal components. It is argued that this gives model 6 more stability across districts, although accounting for a lower R^2 than does model 3. A very good level of predictive power can be achieved from a combination of three predictor variables (psychiatric bed availability, overcrowding 2, and proportion of unskilled workers). To test the appropriateness of the model, residual (observed minus expected) and standardised residual values were calculated and plotted against the outcome variables. The results showed no systematic deviation from a linear model and confirmed that this was a suitable statistical approach to the data.

To summarise the results, Table 5 displays the relationship between the complexity and the predictive power of each model. The results show that each of the derived variables account for less of the variation in the outcome variables (R^2) than do the best individual census variables, the principal components, or the individual census variables combined. Furthermore, these combinations of census variables can effectively account for virtually all the variations in admission rates. Models of increasing complexity, therefore, do indeed better predict admission rates. Clinical, research and planning applications can therefore balance the degree of predictive accuracy desired against the complexity of the analysis required.

Discussion

The major advantage of the small-area analyses performed here is that they employ relatively accessible data, and so can be completed without large-scale data collection. However, they do run the risk of the 'ecological fallacy' – that each individual person is assigned the characteristics of the district of residence. An area-based approach assumes homogeneity within a given geographical area, and this assumption may be misleading or incorrect. Only relatively stable predictor variables therefore should be used, and model performance may improve if multiple rather than single indicators are included (Cagle & Banks, 1986; Liberatos *et al*, 1988). The more widespread use of computerised postcodes may allow such analyses at the electoral ward and enumeration district levels in future (Coopers & Lybrand, 1988).

Hypothesis 1, which stated that psychiatric admission rates for SETRHA will correlate significantly with the Jarman-8 indices, is supported by the results (Table 3). The correlation coefficient values are of the same order of magnitude as those reported by Hirsch (1988) for the North East Thames Region.

Hypothesis 2, which postulated that the Jarman-8 index will better predict SETRHA admission rates than do SMRs, ACORN, Unit9 and Social Index indicators, is not confirmed (Table 3). Both the Unit9 and Social Index variables account for a slightly greater proportion of the variance in admission rates than does the Jarman-8.

Hypothesis 3 stated that the Jarman-8 will better predict outcome than single sociodemographic variables. A comparison of Tables 2 and 3 reveals that many individual variables out-perform all the derived variables. It may be argued that the combined derived variables will prove more robust when applied to larger datasets of, for example, all health districts in England, and future research may test this specifically.

Hypothesis 4 stated that single census variables combined in a multiple regression model will account for a greater proportion of the variation in SETRHA district psychiatric admission rates than either individual or derived variables. This is the case and indeed nine individual census variables will account for more than 95% of such variation in outcome.

Hypothesis 5 proposed that a principal components analysis can identify meaningful components which will predict outcome better than single, derived or previously combined variables. Table 4 shows that three components are identified which account for 92% of the variation within the individual predictor variables, and that they contain census variables which can be entered separately into a further multiple regression equation. However, when the three components themselves are entered into a regression model, although they out-perform the derived variables, they predict less well than the better individual census variables.

Public health implications

The result that many individual census variables are highly correlated with outcome can be interpreted in a somewhat different light: that they indicate characteristics of groups at high risk of psychiatric admission. This approach has implications for health service planning. Patient groups most likely to make relatively heavy use of services can be described (Lavik, 1983), and may warrant specifically targeted services, both to meet their service needs and to free other services for separate patient groups (Richman & Barry, 1985; Tischler *et al*, 1984). Thirdly, these data allow estimates, at the aggregate level, of not only where greater levels of service need exist, but also about the patient groups having a higher proportion of their needs unmet (Shapiro *et al*, 1985; Brewin *et al*, 1987) and this can further guide service development. For this reason the Jarman-8 index is now being used to adjust general practice budgets for local social conditions.

Several specific areas of data collection and access remain inadequate. Firstly, standard data on psychiatric service utilisation should be made readily available by the Department of Health by district of residence. Secondly, data on the receipt of social security benefits would be usable for epidemiological purposes if it were available for health regions and districts. Thirdly, standard reports for utilisation rates should be categorised by diagnosis and by duration of stay. Fourthly, internationally standardised categories for sociodemographic data would allow meaningful comparisons (Kramer & Taube, 1973).

The results presented in this paper indicate that such multiple regression analyses may have the following uses. These models may be used for districts in other health regions, and indeed at more local levels of analysis: that is, electoral wards and enumeration districts. Furthermore, diagnosis-specific rates will allow more precise elaboration of the relationships between exposure and disease, and their possible aetiological implications. Finally, the use of such multiple regression models can be extended to other age and patient groups. Together, these may prove to be rich veins for research in psychiatric epidemiology in the coming years.

Appendix

Elderly alone	Pensioners (men aged over 65, women aged over 60) living alone as a percentage of all people resident in private households.
Over 65	People aged over 65 as a percentage of all residents in private households.
Permanently sick	People economically inactive and permanently sick as a percentage of all people aged over 16 (422/380)
Living alone	All people in a single-person private households as a percentage of all those in private households (1360/1351)
Children under 5	People with children aged under five years as a percentage of all residents in private households
Single parent	People in households consisting of one person over 16 and one or more children under 16 as a percentage of all residents in private households
Unskilled	People in households headed by person in socioeconomic group II as a percentage of all residents in private households
Unemployed	People aged 16 years or over seeking work or temporarily sick as a percentage of all residents in private households
Lacks amenity 1	People in households lacking exclusive use of a bath and inside WC as a percentage of all residents in private households
Lacks amenity 2	People in households sharing an inside WC as a percentage of all residents in private households (944/937)
Overcrowded 1	People in households with more than one person per room as a percentage of all residents in private households
Overcrowded 2	People in households with more than 1.5 persons per room as a percentage of all residents in private households (947/937)
Living in one room	People in private households with one room as a percentage of all persons living in private households (1191/1198)
Population density	Resident population in each district in 1983 divided by district area (hectares)
Changed residence	People aged 16 or over with a usual address one year before the census different from the present address as a percentage of total residents
Ethnic minority	People in households headed by a person born in the New Commonwealth or Pakistan as a percentage of all residents in private households
No car	People in households with no car as a percentage of persons in all households (950/937)

General beds	Number of psychiatric beds available in each district
Nursing home beds	Number of nursing home places available by district

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A Retrospective Case-Note Study of Bipolar Disorder in Old Age

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In a replication of an earlier published study, case notes of 75 elderly in-patients with bipolar affective disorder were examined. Few of the patients had experienced a manic episode before the age of 40. Mean age of onset of affective disorder was 46 years, and first manic episode at 60 years. Cerebral insults before the first manic attacks were recorded in a substantial number of cases, and a family history of mental illness was less common among this group. Bipolar affective disorder is relatively common as a reason for admission of elderly patients.

There is evidence that the prevalence of bipolar disorder decreases with age. Weissman *et al* (1988) in their Epidemiologic Catchment Area Project reported a one-year prevalence rate of 0.1% among 5507 persons over the age of 65, compared with 0.4% for those aged 45–64 years and 1.4% for the age group 18–44 years. They recorded a mean age of onset of 21 years.

Earlier reports commented that onset of bipolar illness is rare after age 60 (e.g. Loranger & Levine, 1978), although Spar *et al* (1979) suggested that the rarity might be partially accounted for by diagnostic inaccuracy. Spicer *et al* (1973) produced evidence that the incidence of mania does not decline with age, and Goodwin & Jamison (1984) reviewed studies showing that later age of onset is associated with increased frequency of relapse. Shulman & Post (1980) purported to dispel the myth that bipolar disorder is rare in old age, but posed a number of unanswered questions. They wondered why so few of their 67 patients (aged 60 or more when admitted) had developed their bipolar illness early in life. Only 8% of their elderly bipolar patients became manic before the age of 40.

Clayton (1981) commented that the number of unipolar patients who finally develop bipolar disease is uncertain. Shulman & Post (1980) called into question Perris's (1966) criteria for unipolar disorder, pointing out the very late age of onset of mania, as well as the large number of depressive episodes and the long latency period before the first appearance of mania, in many of their cases. Stone (1989) reported similar findings in a retrospective study of 92 elderly patients admitted with mania. Clayton (1981) believed that her data confirmed Lewis' (1936) view that as people grow older the intervals between manic–depressive attacks may grow shorter and the attacks themselves longer, but she commented that the question of chronicity in bipolar affective disorder is still unanswered.

The questions raised by Shulman & Post's (1980) study are important and have not yet been satisfactorily answered. Results of longitudinal studies of those who developed the disorder before the age of 40 will be very helpful. Meanwhile, a replication of Shulman & Post's study could be informative.

Method

The psychiatric units at the Prince Henry and Prince of Wales group of hospitals took on responsibility for a catchment area in 1977. These teaching hospitals have over 1000 adult medical and surgical beds, and 100 psychiatric beds. Since 1977 almost all the psychiatric patients sent into hospital on compulsory orders from the eastern suburbs of Sydney (population about 250 000) and most elderly voluntary patients from that area have been admitted to one of the units (see Snowdon, 1981).

During the ten years after accepting this responsibility (i.e. up to October 1987) there were 1833 admissions to the psychiatric units of 1075 persons aged 60 or more who reside in the catchment area. A far smaller number of elderly people from the area (and presumably few elderly bipolar patients) were admitted to other psychiatric hospitals (private or public) during this time. During the same ten years, there were 489 admissions of persons aged 60 or more (346 people) from outside the area, referred because of the units' recognised interest in affective disorders.

The aim of this study was to review in detail the hospital notes of all patients aged 60 or more who were diagnosed as having manic–depressive or bipolar disorder during this ten years and to extract information that could be compared with Shulman & Post's (1980) findings. Names of all patients aged 60 or more were obtained from the admission books of the psychiatric units, and their notes or summaries were inspected (whatever the recorded diagnosis) to ensure that all relevant cases were included in the review. Some cases were excluded, even though at some time a diagnosis of manic–depressive (bipolar) disorder was recorded: cases were included only if there was a history of clear-cut affective episodes which included at least one well documented manic episode lasting at least two weeks. It was required that the patients had all been admitted to hospital at age 60 or over for an affective episode, manic, depressive or mixed; manic episodes could have occurred at any time during the person's lifetime.

Age of onset of the affective illness was determined by the first episode of prominent and persistent mood disturbance, requiring active treatment or intervention. DSM-III criteria (American Psychiatric Association, 1980) were used for diagnosing mania and depression, except that as in Shulman & Post's (1980) study, cerebral organic impairment was not an exclusion criterion. Hypomania and mania are both included under the term 'mania'.

Notes (mainly those kept by registrars in training, but also those of consultants, nurses and other staff and including out-patient and previous in-patient visits) were of a high standard. In occasional cases, relevant data were missing, particularly where patients were admitted for very short periods of time.

Results

A total of 75 cases (52 women, 23 men) were identified as definitely fulfilling the criteria. About 12% of admissions of persons aged 60 or more were because of bipolar affective disorder.

Fifty-four of the 75 cases were resident in the recognised catchment area of the psychiatric units, whereas 21 lived further away. One local resident was admitted 23 times. The mean number of admissions in the ten years of the other 53 area residents was 3.65 (range 1 to 13; 28 were admitted only once or twice). None was in hospital for more than a few months. At a rough estimate, 0.03% of area residents over age 60 (and a similar percentage of those over 65 years) were admitted to the units once or more per year because of bipolar affective disorder.

A further 15 cases (11 from the area, four from outside) were not included even though a diagnosis of bipolar affective disorder had been recorded in their notes. In seven of these cases there was insufficient information in the notes, especially in relation to the history of mania; in five cases the evidence in the notes did not clearly support a diagnosis of mania; in three cases schizophrenia had been diagnosed on all or most other admissions; and in one case dementia was diagnosed at the prior and succeeding admissions.

The following results are for all 75 patients, since no discrepancies were detected between area and non-area patients.

The type of first affective episode was recorded as depression in 46 patients (61%), mania in 13 (17%), mixed in six (8%) and undetermined in 10 (13%). A 'mixed' episode was defined as one where significant depressive and manic signs and/or symptoms were recorded together or alternating during a single affective episode. Of the mixed cases, four out of six were described in the notes as mania *or* mixed.

The mean age at which their first affective episode developed was 46.5 years ($n = 74$), the range being 17 to 73 years; for men the mean was 52.7 years ($n = 23$), while for women it was 43.7 years ($n = 51$ (uncertain in one case)). The exact age of the first manic episode was uncertain in 17 cases (for example, in cases where it was stated that there had been elevation of mood or erratic behaviour for a few days at some time, but the first admission for mania was later), but in ten of these the age of the first such episode could be estimated to within three years with reasonable confidence. Thus the mean age at which the first manic or mixed episode occurred (excluding the seven uncertain cases) was about 58 years (men 62.5 years, $n = 19$; women 56.5 years, $n = 49$). Distributions of age of onset and age of first manic episode appeared unimodal (Table 1). In 45% of cases the first recorded affective episode was at age 50 or later. Figures for area and non-area patients were similar. Furthermore, the sex difference in age of first affective episode and of first manic episode was the reverse of Shulman & Post's (1980) finding, since both occurred earlier among women.

Among those whose first affective episode was a depression ($n = 46$), the mean latency period before the first manic episode was 16.4 years for 32 women (data for three unknown) and 12.0 years for 11 men. The mean age of onset of mania in these cases was about 60 years. Among the 34 cases where the interval between first depression and first (subsequent) manic episode was known accurately, the lapse was 15 years or more in 44% and 25 years or more in 26%, ranging up to 36 years. Of 39 subjects whose first episode was depressive, 54% ($n = 21$) had at least three depressive episodes before their first manic attack, 38% had at least four, and 28% had at least five (in seven cases the number of depressive episodes before becoming manic could not be determined). Moreover, similarly to Shulman & Post (1980), it was found that no elderly bipolar patient whose first attack was purely depressive became manic before the age of 40.

Only three of the area patients and one from outside the area had their first manic attack (none had mixed states) before the age of 40 (at ages 19, 27, 35 and 39), all of these attacks being their first affective episodes. Two of these patients had only manic attacks, but two (those starting at age 19 and 39) had depressions as well. In six of the 75 cases it is not known for certain that they did not have a manic episode before age 40, three being cases where the type of affective swing in their first attacks could not be determined, and the other three starting with depression at ages 21, 27 and 34 with first *definite* manic episodes occurring at 47, unrecorded age, and 42 years.

Table 2 shows that 13 patients were known to have cerebral or neurological abnormalities before the onset of mania. The location of brain damage was not known with certainty in most. One of the 13 had pre-senile dementia. In three additional male cases, abnormalities were recorded (two cerebrovascular accidents, one head injury) but the date of the first manic episode was uncertain; one of the three had a family history of affective disorder. In another male case there was a lengthy history of alcohol abuse and hypoxia, before the onset of mania. Six patients were recorded as developing dementia after onset of mania, four being diagnosed at least 10 years after their first manic episode. Only one had a family history of mental illness. Mean age of onset of their first affective episodes was 53 years, the earliest being at age 41.

Only two of the 13 with a history of cerebral or neurological abnormality before onset of mania had a

Table 1
Frequency distribution of the ages of first affective episodes and of first definite manic or mixed episodes among elderly patients with bipolar disorder

	Age group: years													
	15–19	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75+	Total
Onset of affective disorder (no. of cases):														
male	—	1	—	1	3	2	1	4	4	2	1	3	1	23
female	3	2	3	5	4	7	9	7	4	3	2	2		51
total	3	3	3	6	7	9	10	11	8	5	3	5	1	74[1]
Onset of mania (no. of cases):														
male	—	—	—	—	1		2	1	2	3	3	3	3	18
female	1	—	1	—	1	4	6	9	5	9	8	6		50
total	1	0	1	0	2	4	8	10	7	12	11	9	3	68[1]

[1] Cases omitted if age of onset uncertain.

Table 2
Bipolar patients ($n = 13$) with known cerebral or neurological abnormality (HI = head injury, CVA = cerebrovascular accident, SAH = subarachnoid haemorrhage, RTA = road traffic accident, TIA = transient ischaemic attack) before first manic episode[1]

Sex	Family history of affective disorder	Age of onset of affective disorder: years	Age of onset of mania: years	Age of occurrence of organic condition: years	Comment
M	Yes	60	62	46 & 61	HI at 46, CVA at 61
M	–	70	75	75	CVA
M	–	67	57	54	Alcoholic, pre-senile dementia
M	–	39	66	65	HI
M	–	55	55	54	SAH
M	–	68	68	61	HI
F	Yes	33	62	62	Cardiac arrest
F	–	50	68	60	CVA
F	–	31	50	45	HI
F	–	34	69	58	RTA (unconscious)
F	–	66	66	60	TIAs
F	–	Years ago	63	62	TIA
F	–	17	66	64	Fits after drug withdrawal

[1] In 3 other male cases it was uncertain whether their cerebral abnormality preceded the first manic episode.

recorded family history of affective disorder. In contrast, there was a positive family history in 27 out of 56 cases where no cerebral or neurological insult had occurred before onset of mania ($\chi^2=3.41$, $P>0.05$). Information about family history was lacking in three cases.

Of 73 patients (no relevant data on two), 26 had a recorded history of mental illness and/or suicide among first-degree relatives. Of those nine with a first-degree relative (four fathers, one mother, three children and one brother) who had committed suicide, eight had an onset of affective disorder after age 40; the ninth had depression at age 34.

The vast majority of the patients ($n=69$) had been treated with lithium, although three had to stop because of side-effects. One did not receive it because of heart trouble. Many were still taking it (in 1987), but several others were taking clonazepam or carbamazepine instead.

Of the total 75 patients, 34 were married when first admitted, 21 were widowed, 10 were divorced or separated, and 9 were single (no relevant data in one case). Hysterectomy was performed on 17 of the women (33%) and oophorectomy on a further two, out of 51 (no data on one).

Discussion

This study confirms many of the findings of Shulman & Post (1980). In both these studies of elderly persons with bipolar disorder, the late ages at which the first affective and first manic episodes occurred are remarkable, although in this study the earlier onset among females is the reverse of the 1980 finding. Among those who had depression first, a large proportion had several depressive episodes and many had a long latency period (over 25 years in a quarter of the cases) before the appearance of mania. This supports Shulman & Post's (1980) recommendation for caution before making confident statements that an affective disorder is unipolar.

Paucity of early-onset cases

The mean age of onset of bipolar affective disorder has been reported as about 32 years (Goodwin & Jamison, 1984). Joyce (1984) pointed out that the median age of onset is younger (23 years). Why then was there such a paucity of early-onset cases in the present study and in that of Shulman & Post (1980)? Possible explanations include: (a) premature death of early-onset patients; (b) reduced frequency of episodes requiring hospital admission; (c) admission to other facilities; (d) changed diagnosis; (e) organic cases inappropriately included; and (f) inaccurate recall of age of onset. These explanations are expanded below.

First, premature death may be part of the answer. The mortality rate among manic–depressive patients is two to two and a half times that of the general population although earlier studies found it to be higher (Goodwin & Jamison, 1984); nearly half of them die before the age of 70 years. Weeke & Vaeth (1986) demonstrated the excess mortality among bipolar patients. Tsuang (1978) showed that 6.5% of 92 manic patients died by suicide during a follow-up period of 30–40 years. Angst (1980) followed up 95 bipolar patients for over 25 years, until their average age was just over 60 years; ten had died, but only three by suicide.

Second, Angst (1980) showed no reduction in frequency of affective episodes with age among his series; the majority of cases had not 'burnt themselves out'. However, this contrasts with Grof *et al*'s (1979) view that affective illness sometimes becomes inactive after a number of episodes. Late age of onset appears to be associated with a higher relapse rate (Zis *et al*, 1979), which might account for a higher proportion of such cases among those admitted to hospital. Angst (1980) did not comment on rates of admission to hospital. It would be relevant to know whether, even though his patients continued to have episodes of affective disorder, fewer required admission during such episodes. Maybe after years of experience of a particular patient, doctors can control their affective swings more effectively. It is possible that most such patients only require admission to a psychiatric unit in old age if they have a superimposed organic condition; others have suggested that age-associated changes in the brain may reduce the capacity for manifesting certain signs and symptoms of manic illness (Young & Falk, 1989).

Third, the possibility that early-onset cases were being confined in or referred to other institutions was investigated during the present study. A review in psychogeriatric wards at the nearest mental hospital revealed only seven patients with bipolar disorder who had been in hospital more than a year; none came from the units' catchment area. Involvement by the author in local nursing homes and hostels shows that patients who develop marked mood swings are referred into hospital for treatment. Confinement in such institutions cannot explain the findings.

Fourth, there was no evidence in this study that elderly patients with a history of bipolar disorder were now being diagnosed as having a different condition (e.g. dementia or paranoid state). Notes and/or summaries of all elderly persons admitted to the units were carefully perused with this possibility in mind.

Fifth, some might question whether cases where organic brain changes were noted should have been included among the bipolar cases in both Shulman

& Post's and the present study. However, excluding them makes the paucity of female early-onset cases in the present series even more striking.

The sixth possibility is that the age of onset of affective disorder was incorrectly recorded in the notes. It may be that patients and their relatives were inaccurate in their recall of previous episodes of admissions, or that doctors did not seek or record appropriate information. Joyce (1984) interviewed 66 bipolar patients and found that six had depressive episodes before the first affective episode recorded in their case notes, although only one had received earlier out-patient treatment; another had an unrecorded earlier hospital admission. It is known that case notes at the hospitals and units where Shulman & Post (1980) and the present author carried out their studies were of a high standard. It seems likely that relevant available information concerning prior affective episodes was recorded in most cases. However, in a number of cases in the present study, patients and informants were recorded as being uncertain or vague in their recollection of early affective symptoms. Goodwin & Jamison (1984) point out that manic–depressive patients not uncommonly have histories of labile mood for several years before the onset of a definitive episode. Where information was uncertain in the present study, analyses were made with the data excluded and then included.

Further longitudinal studies of middle-aged patients with early-onset bipolar disorder are desirable to try to better elucidate the reasons for the paucity of early onset cases among elderly bipolar patients in hospital.

Organic conditions before mania

Shulman & Post (1980) reported that a considerable proportion of their bipolar patients had cerebral organic disorders before the onset of their mania. The proportion in the present study was similar, but without the male preponderance. It could be appropriate to consider some of these to be cases of secondary mania; this term was used by Krauthammer & Klerman (1978) to describe manic syndromes associated with antecedent physical illness or drugs. They found their patients had a later age of onset and (where known) no family history of bipolar disorder. In the present study, those with cerebral organic impairment before the onset of mania were less likely to have a family history of mental illness. Stone (1989) found persisting clinical evidence of cerebral organic impairment in 22 of 92 elderly patients admitted with mania, but only two had a family history of affective illness. By contrast, Starkstein & Robinson (1989) reported that four of nine cases of post-stroke mania had a family history of affective disorder.

In four of the 13 cases detailed in Table 2 a diagnosis of organic affective syndrome (called organic mood disorder in DSM–III–R) might have been considered, since they had no history of affective disorder themselves or among family members before the organic disorder. Three of these had recurrent manic episodes, with long intervening periods of euthymia. The fourth (case 11) had a single depressive episode and then a manic episode, some years after first developing cerebrovascular disease. In the other nine cases the pattern of depressive swings before their organic disorder makes it appropriate to record a change of diagnosis from unipolar to bipolar disorder, rather than from unipolar to organic mood disorder.

In one case, cardiac arrest (and consequent cerebral anoxia) preceded first onset of mania (Table 2). Several further depressive episodes and another manic episode occurred during the next five years. Kumar & Agarwal (1988) reported a 32-year-old man who developed affective disorder, initially manic, six months after cardiac arrest.

Epidemiology of bipolar disorder in old age

A majority of the present sample were resident in a recognised catchment area, and the sample included those admitted compulsorily and those initially admitted to medical and other wards. A number of bipolar cases were included in the study even though the type of the first affective episode was uncertain. It is likely that most elderly residents of the catchment area who were admitted to hospital during the ten years because of bipolar disorder have been included in the study. The composition of Shulman & Post's (1980) sample may have been more subject to selection factors, although the findings in theirs and the present study were remarkably similar.

The hysterectomy rate in the present sample (33%) was somewhat higher than age-specific hysterectomy rates in New South Wales (25% at age 70, 28% at age 80) (Dickinson & Hill, 1988); examination of the influence of sociodemographic factors has not been possible.

From the present study it is estimated that at least 0.03% of area residents over the age of 65 are admitted to hospital once or more per year because of bipolar affective disorder. In this part of Sydney, 12% of elderly admissions to psychiatric units are for treatment of bipolar disorder. The percentage treated as out-patients or in the community or by general practitioners, the percentage admitted to private or non-area hospitals, and the percentage untreated, have not been estimated. The evidence is that bipolar affective disorder is a common problem among elderly people referred for psychiatric treatment.

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Bulimia Nervosa: Family Size, Sibling Sex and Birth Order

A Catchment-Area Study

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Family size, sex of siblings and birth order were examined in 225 bulimic patients of normal weight, all stemming from the same circumscribed catchment area. Although bulimia can occur in any size family, all-female sibships were significantly over-represented. In small families at least, the bulimic patient was highly likely to be the only or eldest daughter. In small sibships, a bulimic who was first-born was significantly more likely to have a younger sister; if second-born she was more likely to have an elder brother. Despite the very large sample size, no final conclusion can be made on birth order.

Herzog (1982) found, *inter alia*, no differences in birth order in a small comparison study between normal-weight bulimics and anorectics, although he did find a greater number of only-children among the bulimics. This supports the first author's clinical impression (Lacey, 1984) that many bulimic patients of normal weight are the eldest or only daughters and that during times of parental marital discord, the mother can use her daughter as an easily available 'therapist' (Lacey *et al*, 1986). The aim of this study is to examine birth order and sibling systems in a substantial sample to determine if a particular family structure is associated with subsequent bulimia.

Two previous studies have reported, among other demographic variables, mean birth order (Weiss & Ebert, 1983) or birth order (Dolan *et al*, 1989). In terms of such studies, all have been on very small samples and the lack of significant findings is not surprising. The paucity of such studies in bulimia belies a confusing array of reports on anorexia nervosa populations. These studies have indicated an excess of female siblings (Cobb, 1950; Dally, 1969; Theander, 1970; Bruch, 1973; Hall, 1978), with the exception of Crisp (1970) who found the converse and Garner & Garfinkel (1982) who found no excess of siblings of either sex over the other. To complete the confusion, some workers report that only-children are over-represented in anorectic populations (Kay *et al*, 1967) while others have disagreed (Rowland, 1970; Halmi, 1974).

The results of studies of birth order in anorectic populations have been equally inconsistent, showing an excess of first-born (Rowland, 1970) or later-born (Crisp, 1977; Crisp *et al*, 1980), or indicating that an anorectic patient may be found in any ordinal position within the family (Theander, 1970; Hall, 1978; Garfinkel & Garner, 1982).

A more recent study of anorectics brought up in small sibships of two (Gowers & Crisp, 1987) showed a non-significant association between the presence of a male sibling and the bulimic subtype of the condition. A patient's birth-order, however, has no effect on the presence or absence of binge-eating in anorectics (Garfinkel *et al*, 1980; Vandereycken & Pierloot, 1983; Gowers & Crisp, 1987).

Method

The circumscribed catchment area studied was the London Boroughs of Wandsworth and Merton: a population of 375 000 persons. Only patients referred by a doctor were seen. It is the belief of the authors that it would be very rare indeed for bulimic patients to be referred elsewhere: the clinic is well known to local general practitioners (GPs), all patients from the district were, and are, accepted without quibble, and referrals to a catchment area's general psychiatrist would have led to onward re-referral to the bulimia clinic.

Bulimia overwhelmingly occurs in women and only female patients are considered in this study. Patients completed an extensive demographic and clinical-theory questionnaire which forms a general database beyond this study, and were then interviewed by the first author. All patients were diagnosed by the first author as having bulimia according to the criteria of DSM–III–R but excluding patients who had anorexia nervosa, in accordance with the criteria set down by Crisp (1980), or who had massive obesity (over 150% mean-matched population weight).

The patients in this sample were accompanied by their mothers who were also interviewed. The patient was seen first and alone, and then the mother was seen alone. Details of family structure and birth order were gained from both, in particular the number of siblings in the family, the birth order, and the gender and position of all siblings.

Analysis

A patient's ordinal position in her family may be expressed by the figure m – 1 divided by n – 1, where the patient comes mth in a sibship of n, that is, the total number of children borne by her mother. This expression varies in value between

0 and 1 with a mean value which, in a random collection of individuals, tends towards 0.5 (Slater, 1962). When using Slater's formula, only-children should be ignored. Not only the mean ordinal position, but also the variance and standard error of a series are calculated, to see if the mean differs significantly from that expected, using normal distribution methods for large samples.

When examining the relationship between sibship and position (or gender of sibling), χ^2 tests with Yates' correction were used. Where our observed distribution of all-female sibships was compared with that expected a χ^2 'goodness of fit' test was used.

There are so many variables acting on the structure of the family that it could be argued that if a patient's siblings were to have a particular effect on the aetiology of bulimia, then the maximum impact would be seen in a sibship of two, that is, where the patient has one sibling. Sibships of two are examined separately.

Results

The average family size, that is, the number of children was just less than three (2.93, range 1–5), the patients reporting a total of 433 siblings.

Table 1 shows the distribution of birth order for the 225 patients. A total of 103 patients (45.7%) were the eldest ($n = 89$) or only-child ($n = 14$), and 76 patients (33.7%) were the youngest in their families. In addition, there were 50 patients who had older brothers, making a total of 153 patients (68%) who were the eldest or only female child in their families.

The mean ordinal position of the patients was 0.475 (variance = 0.2016, s.e.m. = 0.0438). The difference from the expected mean of 0.5 is not significant.

Of the 433 siblings, 233 were sisters and 200 brothers. It follows that, including the patients (all of whom were women), these bulimic *families* were marked by having more female siblings: 458 girls and 200 boys. The most common male (M) and female (F) sibling systems and size of families were, in order: F/F (45 families); M/F (22 families); F/F/F (20 families); F (14 families); F/M (14 families); F/M/F (12 families); M/F/F (10 families). Eighty-eight families had other configurations.

The patients were not more likely to have an older or a younger sibling of either gender: 212 siblings were older, 104 of whom were sisters and 108 brothers; 221 siblings were younger, 129 of whom were sisters and 92 brothers ($\chi^2 = 0.065$, with Yates' correction $\chi^2 = 3.4$).

Table 1
Distribution of birth order

Sibship size	Total no. of families	Patients' order within sibship 1	2	3	4	5
1	14	14				
2	81	49	32			
3	62	20	14	28		
4	44	10	12	14	8	
5	24	10	2	0	4	8
Total	225	103	60	42	12	8

Table 2
Distribution of all-female sibships among families with sibship size of two or greater, and comparison with expected distribution

Sibship size	Total no. of families	No. of all-girl sibships	Probability of all girls[1]	Expected no. of all-girl sibships
2	81	45	1/3	27.0
3	62	20	1/7	8.86
4	44	6	1/15	2.93
5	24	2	1/31	0.77
Total	211	73		39.56

χ^2 goodness of fit test: $\chi^2 = 31.1$, d.f. = 3, $P < 0.001$.

1. Probability of all girls given at least one girl.

Eighty-seven patients (38.6%) came from an all-female sibship: there were 14 'only' children, 45 families with two girls, 20 families with three girls, six families with four girls and two families with five girls.

Table 2 shows the distribution of all-female sibships among the 211 families having a sibship size of two or greater. The probability of having an all-female family, given there is at least one girl, and ignoring the position of the bulimic female, is given in the fourth column. Thus for a three-sibship family, the possibilities are MMF, MFM, FMM, MFF, FMF, FFM and FFF, and the probability of having three girls, given that at least one is a girl, is 1/7. The expected number of all-girl families, given the total number of families of each sibship size, is given in the fifth column. The distribution observed is different from that expected, and all-girl siblings are significantly over-represented ($\chi^2 = 31.1$, d.f. = 3, $P < 0.001$) (Table 2).

Cases in which the bulimic child was a member of a small sibship of two children were examined further to see if patterns were more evident in these smaller families. Eighty-one families contained two children only and the bulimic children were more likely to have been first-born ($n = 49$) than second-born ($n = 32$). They were as likely to have a brother ($n = 36$) as a sister ($n = 45$). However, a bulimic who was first-born was significantly more likely to have had a younger sister ($n = 35$, 72%) than a younger brother ($n = 14$, 29%) and a bulimic who is second-born is more likely to have had an elder brother ($n = 22$, 69%) than an elder sister ($n = 10$, 31%) (χ^2, with Yates' correction = 11.02, d.f. = 1, $P < 0.001$).

Table 3
Comparison of social class distribution of bulimic women and the local population from which they stem

Social class	Bulimia clinic	Local population[1]
I	3.6	2.1
II	24.5	22.9
III	48.6	51.6
IV	16.3	14.5
V	0	4.8
Unclassified	12.0	4.0

1. Source: Office of Population Censuses and Surveys (1982).

The mean age of the sample was 24.6 years (s.d. = 4.6; range 16–40 years). The mean weight was 60.6 kg (s.d. = 8.6). The mean-matched population weight (Kemsley, 1953) was 104.9% (s.d. = 14.1). Three-quarters of the patients were unmarried, 22% were married and 4% divorced. Over three-quarters of the clinic stem from social classes I, II and III with 48% from social class III. Twelve per cent were unclassified, being mainly students. Table 3 shows that the social class distribution is similar to the social class of the catchment area (Wandsworth and Merton: Office of Population Censuses and Surveys, 1982).

Discussion

This is a clinical study whose strength is that the information was gathered by a single clinician, who was well versed in the condition and who worked hard to establish an alliance such that the patient and her mother would feel at ease. The data were supported by similar questions in a questionnaire completed before the interview. In almost all cases, the patients subsequently went into treatment (Lacey, 1983; Lacey, 1986) in which family matters were further explored. This study is based on data derived from the largest clinical-interview population of bulimic patients.

The criticism often levelled at birth-order studies, that the population is highly selected, is not valid in this case. The population was from a defined catchment area and there was no attempt to accept patients who were 'severe' or 'interesting' – and in particular, no tendency to take twins, etc. Further, the data were not based on the memory of the patient alone: in all cases the patient's mother was used as an informant and she was interviewed in the absence of the patient. However, it has to be accepted that a mother could have reasons for suppressing knowledge of early pregnancies or not wanting to release it in this way. The sample is representative of a clinic population unselected by advertisement, payment or 'special centre' bias; of course, it does not claim to be representative of the total spectrum of the disorder in the community.

This study shows that bulimia may occur in a range of sibships. To the casual eye, sibship size does not appear to be different from the general population; further, bulimic women are no more likely to have older or younger siblings of either sex. It would be surprising if such a basic finding were evident at a statistically significant level in what is, in terms of birth order studies, a small population.

Bulimic families are marked by having more daughters than sons: 458 girls and 200 boys. This is to be expected as all the patients were women and such siblings were significantly over-represented. Nonetheless, including the 14 only-children, 87 patients came from all-female sibship families. The authors would not postulate that this is causative in any way. Bulimia is multifactorial in aetiology and research such as this can only indicate possibilities, but the impression was gained in treatment that these families were, more particularly than the rest, concerned with aspects of appearance and presentation.

It has been argued that the maximum impact of any variable would be seen in a sibship of two – that is, where the patient has only one sibling. There were 81 such families among the patients in the study. The data show that these 81 bulimic women were more likely to have been first-born than second-born. They were just as likely to have a brother as a sister although, if the bulimic was first-born, she was significantly more likely to have had a younger sister than a younger brother. If she were second-born, she was more likely to have had an elder brother than an elder sister; in other words, she was still likely to be the elder daughter.

This supports the first author's clinical impression that patients tend to be the eldest or only daughter, with the implication that as a young adolescent, she is used by her mother as an unwilling or, at least, the most easily available therapist. Certainly this is commonly reported in the clinic: the patient describes how her mother, herself depressed and/or within a difficult marriage, unburdened herself to her daughter at an age when she was quite unable to deal with the expressed emotions. However, the author would emphasise that there is no substance to make the point more earnestly than this without a substantial increase in sample size; furthermore, the finding is open to other interpretations.

No correction has been – or can be – made in this study for incomplete sibships but this is unlikely in a group whose mean age was 25 years. Such important variables as age-gap between siblings, or even whether the sibling was living at home or not, could not be taken into account. Slater's Index argues that the expected mean birth-order of a population is, or probably more accurately, tends to 0.5. It is incorrect to assume that for a given subject her chance of being earlier or later born within the sibship is equal. The mean birth order of a population as a whole taken from any one year varies depending whether the population is increasing or decreasing, or if there is an increasing rate of starting new families (Price & Hare, 1969). Most of the patients in this series were conceived during the early sixties and no profound politico-economic changes were occurring then which would support such reservations. A related issue concerns the sex of this population. Although it is probable that a family is thought to be as complete after the birth of a girl as of a boy, this is not necessarily so.

A relationship between psychiatric disturbance and birth order may hide the fact that the real relationship is with a variable which correlates with birth order, such as maternal age or bereavement or birth weight. Much of the value of the findings of clinical birth-order studies have been questioned and this study highlights the methodological problems. The biases which may distort observed distributions of patients by birth rank have been discussed by Price & Hare (1969). It is unlikely that a more pertinent analysis of the association between bulimia and family systems and birth order could be gained without a sample size of at least the square of that in this study!

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Anorexia Nervosa: Outcome and Prognostic Factors after 20 Years

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Forty-one patients with anorexia nervosa, admitted to the Maudsley Hospital between 1959 and 1966, were followed up after a mean of 20 years. An assessment of general outcome (based on the Morgan-Russell scales) yielded three outcome categories: 'good' ($n = 12$), 'intermediate' ($n = 13$) and 'poor' ($n = 15$). Six patients (15%) had died from causes related to anorexia nervosa; at least 15% had developed bulimia nervosa. There was a general consistency between the follow-up at 20 years and that previously conducted five years after admission, although with a few individual patients there were serious prognostic errors at the earlier follow-up. A poorer outcome was associated with a later age of onset, a history of neurotic and personality disturbances, disturbed relationships in the family and a longer duration of illness.

Anorexia nervosa is an illness that frequently follows a protracted course. In spite of this, most published studies on outcome have relied on relatively short follow-up periods. There are only a few studies in which patients have been followed up after 10 years or more (Tolstrup *et al*, 1985; Halmi, 1988) or even after 20 years (Farquharson & Hyland, 1966; Theander, 1985). Moreover, there are difficulties in interpreting the results of many of these studies because of shortcomings in methods and information-gathering. The problems in making comparisons between studies have been discussed by Hsu (1980), Schwartz & Thompson (1981) and Steinhausen & Glanville (1983).

The weakest aspect of any follow-up study in anorexia nervosa is that it relies on a selected group of patients often referred to a specialist hospital clinic. The proportion of patients who recover, become chronically ill or die must vary from one population to another. In the study that we are reporting, the selection of patients was such that the results are likely to err on the side of chronicity and higher mortality.

In spite of these difficulties, follow-up studies provide valuable information about the long-term course of the illness and can reveal factors predictive of the eventual outcome.

The present study is a long-term follow-up of the same cohort of patients who were previously followed up by Morgan & Russell (1975) after an average of five years (not less than four years). The aims of this study were to determine:

(a) if a long-term follow-up confirmed the findings of the five-year follow-up
(b) if the factors that were prognostically significant at five years were sustained in the prediction of outcome at 20 years.

Methods

This study comprises a series of consecutive admissions (38 women, three men) to the Maudsley Hospital between November 1959 and October 1966 with a diagnosis of anorexia nervosa. They were followed up in 1983–84: not less than 18 years and an average of 20 years after admission. All the patients satisfied the diagnostic criteria for anorexia nervosa as defined by Russell (1970), and utilised by Morgan (1973) and Morgan & Russell (1975) in their five-year follow-up study. At the time of admission the mean body weight was 64.28% (s.d. 9.2) of average body weight (ABW; Society of Actuaries, 1959). Some of the patients had been ill for several years, and the mean duration of the illness was 3.7 years (s.d. 3.7). This was therefore a series of patients who were severely undernourished with prolonged illnesses. The mean age of onset was 18.0 years (s.d. 6.7) and the mean age on admission was 21.5 years (s.d. 8.6). Most of the patients had a number of neurotic or abnormal personality traits and nearly half had had previous psychiatric treatment. Further details can be found in Morgan (1973), Morgan & Russell (1975) and Ratnasuriya (1986).

Procedure

The case notes were analysed for factors which, from the review of the literature, were thought to be of possible prognostic significance. The presence or absence of these factors in the case notes was noted, or rated on a 'yes' or 'no' basis or quantified if possible (see Ratnasuriya, 1986).

Five-year follow-up data were obtained from Morgan (1973) and Morgan & Russell (1975). Collection of the 20-year follow-up data posed practical difficulties and a great deal of attention had to be paid to tracing the patients. This was usually done through the Family Practitioner Committee central register and the patient's general practitioner (GP). A letter and form were then sent to the patients to find out whether they were willing to participate in the study. Where necessary, the next of kin were traced in a similar way and the patients contacted through them.

In this way information was obtained on all but one of the original 41 patients. This patient lived in the USA and did not reply to letters sent to her through her mother.

Twenty-four patients (58%) were interviewed by the first author. Seven patients had died. Six patients (four of whom lived abroad) returned a detailed questionnaire and this information was always corroborated by interviewing the GP or a relative. Total reliance on the GP was needed with the four remaining patients.

The clinical data thus obtained were then rated using the Morgan & Russell scales (1975). These are 14 scales covering a number of areas of the patient's functioning. The ratings on these scales are combined to provide scores (from 0 to 12) on nutritional status, menstrual function, mental state, psychosexual adjustment and socioeconomic functioning (Morgan & Russell, 1975; Morgan & Hayward, 1988). From these a final score – the average outcome score – is computed. An overall rating of general outcome was also made in which each individual was categorised as having one of the following three outcomes:

(a) good outcome – normal body weight (100 ± 15% ABW) with normal menstruation
(b) intermediate outcome – normal or near normal weight (75–100% ABW) and/or menstrual abnormalities
(c) poor outcome – low weight and absent or scanty menstruation

This overall classification was kept for purposes of comparison with the earlier study. It has the disadvantage that it does not give an accurate assessment of outcome for patients in whom the illness has progressed from a restricting form of anorexia nervosa to bulimia nervosa. In such patients weight and menstrual function can give a misleading picture unless they are accompanied by an assessment of the frequency of episodic overeating and self-induced vomiting. For the second (prognostic) part of the study an additional criterion was included: patients who were overeating or vomiting (weekly or more) were classified as having a poor outcome regardless of their weight or menstrual status. The overall outcome data are presented using both the original and the modified criteria.

The patients themselves were asked to rate their own progress since leaving hospital on a scale from 0 (worse) to 3 (recovered). A total duration of the illness was calculated for each patient, this being the length of time from the onset of the illness (usually the date of cessation of menstruation) to the time that the patient fully or at least partially recovered without further relapse, or (in patients with a poor outcome) the time of the final follow-up interview or the time of death.

Results

The average length of follow-up was 20.2 years (s.d. 2.0). The average age of the patients at the time of follow-up was 40.9 years (s.d. 9.5).

Table 1 shows the categorisation of the patients into the three outcome groups using both the original and modified criteria described above. For the time being we confine ourselves to the original criteria.

Table 1
General outcome at 20 years

Outcome category	Original criteria *n*	(%)	Modified criteria *n*	(%)
Good	12	(30)	11	(27.5)
Intermediate	13	(32.5)	12	(30)
Poor				
chronically ill	8	(20)	10	(25)
dead	7	(17.5)	7	(17.5)

Twelve patients had recovered from anorexia nervosa in that both their weight and menstrual function were normal. However, difficulties with eating tended to persist and only four patients could be said to eat quite normally. Excessive preoccupations with thoughts of weight and body shape also continued to be prominent in five of the twelve. Their average weight at follow up was 91.8% ABW (s.d. 6.2). Eleven of them had married. Two, while recovered from anorexia nervosa, had become dependent on alcohol. One woman had remained socially isolated and unhappy and one patient had episodic overeating and vomiting.

Thirteen patients had an intermediate outcome. Their mean weight at follow-up was 83.4% ABW (s.d. 9.9). Five of them were well in all respects except for their weights of 78.9% to 83% ABW (including one who had had a partial gastrectomy and had a body weight of 82.3% ABW but was otherwise well). Eight subjects showed some disturbance in their pattern of eating (e.g. restricting food, avoiding regular meals or maintaining a very rigid diet). Six of these also expressed exaggerated fears about their weight and body shape. The intermediate outcome group included one male patient (aged 37 years) who had a very low libido and had refrained from sexual activity for many years. Eight of this group were married. As in the previous group one patient had developed bulimic symptoms.

Eight patients were chronically ill at the time of the follow-up, with a mean weight of 60.7% ABW (s.d. 12.1). They all reported severe restriction of their diet and seven were worried about their appearance. Six were vomiting regularly and of these three were also overeating at least once a week.

Seven patients had died during the 20-year follow-up.

Table 2 shows the patients' weights at follow-up and also the mean outcome scores (out of a possible of 12) on the five main Morgan/Russell scales. This table also compares these measures for the patients in the three outcome groups. The classification of patients into the three outcome groups is only partly borne out by the more detailed clinical ratings. While there is an overall statistically significant difference (using a one-way analysis of variance) between the outcome groups on all the scales, this difference is principally due to the low ratings of patients in the poor outcome group. The scores of the patients in the good and intermediate outcome groups closely resemble each other and differ significantly only in weight.

On self-progress ratings, 16 of the patients (nearly 50% of those still alive) considered themselves to have recovered. With two exceptions these were subjects who were classified by the interviewer as having a good or

Table 2
Mean weight and scores on Morgan & Russell (1975) clinical scales of patients at 20-year follow up in the three outcome groups

		Outcome groups			One-way analysis of variance		
	All patients	Good (G)	Intermediate (I)	Poor (P)	Overall *P*	Contrast	
						G+*I* v. *P*	*G* v. *I*
Mean (s.d.) weight: % ABW	80.4 (15.5)	91.8 (6.2)	83.4 (9.9)	60.7 (12.1)	0.0001	0.0001	0.02
Mean (s.d.) score on Morgan & Russell scales:							
nutritional status	6.3 (4.2)	8.4 (3.5)	7.6 (3.3)	1.8 (2.8)	0.0001	0.0001	NS
menstrual function	8.7 (4.7)	12.0 (0)	10.8 (2.2)	2.2 (2.7)	0.0001	0.0001	NS
mental status	9.1 (3.7)	10.3 (3.2)	10.6 (3.0)	5.3 (2.8)	0.0005	0.0001	NS
psychosexual adjustment	8.7 (4.1)	11.0 (2.1)	9.7 (2.9)	4.3 (4.5)	0.0001	0.003	NS
socioeconomic status	8.1 (3.8)	9.1 (3.1)	9.4 (3.4)	4.9 (3.4)	0.008	0.006	NS
Average outcome[1]	8.3 (3.3)	10.1 (1.6)	9.6 (2.3)	3.8 (1.9)	0.0001	0.001	NS

1. Calculated from the five main Morgan & Russell scales.

intermediate outcome. The other two cases had clearly not recovered but were unwilling to accept that this was the case. The self-progress rating correlated highly with the average outcome score made on the basis of the interviewer's clinical assessment ($r = 0.83$, $P < 0.01$).

Even among those whose outcome was generally good, a third were regularly restricting their diet and a third reported eating irregularly. Among them some reported, for example, that they avoided eating regular meals unless pressured by their husbands, often restricting themselves to irregular 'snacks'. Others found that they were only able to maintain their weight if they kept to a very rigid diet. Excessive preoccupations with thoughts of food and weight also tended to persist, being reported by over half of the patients who were otherwise doing well. Bulimia was relatively uncommon in this series of patients. Over the 20 years, five patients (of the 34 who were alive at follow-up) would have warranted a diagnosis of bulimia nervosa as described by Russell (1979). This may be an underestimate, as the figure does not include patients who developed bulimia nervosa before their death. Thus an estimate of the frequency of this complication would be at least 15% (five out of 34). Six further patients exhibited bulimic behaviour short of the full syndrome: vomiting was reported by six of the patients in the poor outcome group and one in each of the other groups.

Among the 30 live female patients, 22 were menstruating, of whom three had irregular periods. Eight had amenorrhoea at follow-up which had persisted since admission. There was a clear relationship between weight and menstrual function. All the patients whose weight was below 75% ABW reported amenorrhoea and conversely those whose weight had risen above 75% ABW were menstruating (with the exception of one woman weighing 78% ABW).

Attitudes to sex were varied but in general there was a clear relationship with overall outcome. Nineteen patients said they had a satisfactory sexual relationship but eight patients avoided any sexual contact. Nine were reluctant to get married and three said that even if they were married they would not have any children. Of the whole group just over half ($n = 21$) did get married and 17 of them had children. Out of a total of 38 children 14 were girls and 24 boys. The majority of the children ($n = 29$) were conceived when their mothers were quite thin (i.e. less than 85% ABW). In five cases the mothers had irregular periods and three pregnancies occurred when the mothers were amenorrhoeic.

Emancipation from the family of origin was another problematic area. In spite of their age, ten patients reported a strong dependence on their families of origin. For instance one patient, herself married, would telephone her mother every day for support and to bid good night. The patients' social contacts and activities tended to be restricted, and one third led very isolated lives. The employment of the patients was also affected and fewer than half ($n = 16$) were employed. It was striking that among the 13 unmarried patients only four were employed. Again, the patients most strongly affected were those in the poor outcome group, who were likely to be single and unemployed.

Three patients had been abusing alcohol regularly over a number of years. One had given birth to a child who was suffering from the foetal alcohol syndrome. Two other patients had previously abused alcohol but during the past few years had stopped. Two patients reported dependence on prescribed drugs and three abused laxatives.

Of the seven deceased patients, two had died by the five-year follow-up, one from suicide and the other from a combination of nutritional deficiencies. Five further deaths had occurred by the 20-year follow-up. It is noteworthy that among these five deaths only two were from the 'poor outcome' category, whereas two were from the 'intermediate outcome' and one from the 'good outcome' (all as originally judged at the five-year follow-up). Of the six deaths attributable to anorexia nervosa, three were due to suicide and three to complications of the illness associated with electrolyte imbalance. The seventh death was due to unlawful killing by a stranger. Excluding this last patient, the crude death rate (i.e. not corrected for expected deaths) after a mean follow-up of 20 years was 15%.

At the time of the follow-up many of the patients ($n = 15$) had definite depressive and/or neurotic symptoms. During the course of the 20 years, 19 patients had had further psychiatric treatment (10 for eating disorder, five for minor depressive illness, one each for bipolar affective psychosis,

Table 3
Comparison of outcome at the five-year and 20-year follow-up

	20-year follow-up				
	Good	Intermediate	Poor		Total
			Ill	dead	
Five-year follow-up					
Good	6	8	1	1	16
Intermediate	4	3	2	2	11
Poor					
ill	2	2	5	2	11
dead	–	–	–	2	2
Total	12	13	8	7	40

obsessive–compulsive neurosis, agoraphobia and alcohol dependence). This included all the patients who remained chronically ill and approximately half of the patients who eventually recovered at least partially.

Comparison with the five-year follow-up study

Table 3 compares the overall outcome of the patients at the two follow-up points. The difficulty in distinguishing between good and intermediate outcome in the long-term has already been mentioned. Taking that finding into account, a clear pattern emerges from those who did well at the earlier follow-up. Out of 27 patients in the good or intermediate outcome groups at five years, 21 continued to do well, but three patients had become chronically ill and three had died. Seven out of 11 patients with a poor outcome at five years remained seriously ill or had died, but four had improved (Table 3) by the 20 year follow-up.

The overall clinical rating of outcome as measured by the average outcome score of the Morgan/Russell scales provides a finer comparison. A strong correlation ($r=0.66$, $P<0.01$) was found on this measure between the two follow-ups.

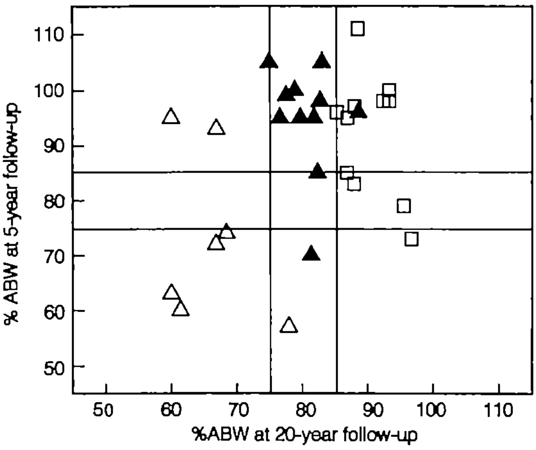

Fig. 1 Comparison of % average body weights (ABW) at the five-year and 20-year follow-up for those with good (□), intermediate (▲) and poor (△) outcome at 20-year follow-up ($r=0.36$; $P<0.05$) (five bulimic patients with wide fluctuations in weight and all patients who died are excluded).

A comparison of body weight at the two follow-ups (Fig. 1) offers, perhaps surprisingly, a less clear picture. Overall there appears little association between the weights at these two points in time. However, this is partly due to the fact that in five patients (who had developed bulimia nervosa), weight fluctuated between extreme emaciation and obesity. When these patients are excluded from the analysis (as in Fig. 1), a statistically significant but modest correlation is found ($r=0.36$, $P<0.05$). A closer inspection of the scattergram in Fig. 1, however, reveals a fairly consistent pattern closely related to the final categorisation of the patients into the good, intermediate and poor outcome groups. Patients with extremely low weights (below 75% ABW) at five years generally remained thin and with two exceptions were rated as having a poor outcome at 20 years. The four patients whose weight had been in the range of 75%–85% all improved. Finally, the patients whose weight had been normal (within 15% of ABW) at five years had (again with two exceptions) maintained their weight sufficiently to be classified as having a good or intermediate outcome.

Predictors of outcome

We mentioned earlier that for the purpose of this final evaluation the criteria for classifying general outcome were adjusted to take into account bulimic symptoms. Two patients (one each in the good and intermediate outcome groups) are affected by this change, and on these new criteria are classified as having a poor outcome (Table 1).

As can be seen from Table 4 the age of onset of the illness as measured by the onset of amenorrhoea remains a very strong predictor of outcome even after 20 years. Of the 11 patients whose illness started at or after the age of 18 years only two improved or recovered and the rest either remained chronically ill ($n=6$) or died ($n=3$). Conversely, of the 18 patients with an onset of illness between 11–15 years only two had a poor outcome. The mean age of onset of the illness for the patients in the good and intermediate outcome groups was 14.9 years whereas patients with a poor outcome became ill on average at 21.5 years ($F=15.7$, $P<0.0001$).

The duration of illness at the time of the key admission ($\bar{X}$) showed a somewhat weaker but still significant association with final outcome of good (G), intermediate (I) or poor (P) ($\bar{X}_{G+I}=2.1$, $\bar{X}_P=5.2$, $F=4.6$, $P<0.04$ – analysis of covariance with age of onset as a covariate).

Table 4
Age of onset (measured by onset of amenorrhoea) and outcome at 20 years

Age of onset: years	Outcome Good n	Outcome Intermediate n	Outcome Poor n
11–15	7	9	2
16–17	3	2	6
≥18	1	1	9

$\chi^2=15.3$ $P<0.004$

Table 5
Pre-morbid prognostic factors and outcome at 20 years (all patients)

	Outcome			
	Good ($n=11$)	Intermediate ($n=12$)	Poor ($n=17$)	Fisher test ($G+I$ v. P)
Neurotic traits in childhood	2	4	9	0.08
Personality difficulties	6	6	16	0.004
Disturbed relationships within the family	4	3	15	0.0003
Two or more of the above	4	5	16	0.0004

Table 5 examines the pre-morbid factors related to outcome. It shows that a history of poor individual adjustment and a disturbance in family relationships are also indicative of a worse prognosis.

We repeated this last analysis excluding patients with a late onset of the illness (18 years or over) in view of the strong association of age of onset with outcome. The relationship with outcome remained quite strong even for this smaller group of patients whose prognosis is generally more favourable. Of the eight patients with a poor outcome in this group, seven scored positively on at least two of the three factors (Fisher's test, $P=0.01$).

As was discussed in the previous section, a good outcome at the five-year follow-up was also a strong indicator of the long-term outcome.

We have already presented data showing that the duration of illness at the time of the key admission to hospital is predictive of outcome. However, the length of illness is not a constant factor as it changes with time, so that examining the relationship between the duration of illness and the probability of an eventual recovery in this way is not the most appropriate approach. In a long-term study such as this one a more complete picture is obtained by analysing the course of the illness over the whole observation period. Statistical techniques known as survival methods (Isager *et al*, 1985; Kalbfleisch & Prentice, 1980) allow the analysis to take into account the fact that the length of follow-up varies between patients and also that the size of the sample gradually diminishes over time. Fig. 2 illustrates the course of the illness over the follow-up period. For the purpose of this analysis the good and intermediate outcome groups are combined (termed 'recovered'). A survival analysis indicates that initially there is a fairly constant rate of 'recovery' (approximately 15% of those still ill in every successive three year period). After 12 years the recovery rate starts to reduce, dropping sharply to less than 7% after 15 years. Nevertheless, even after this time some patients continue to recover. Fig. 2 also illustrates the death toll increasing to six deaths attributable to the illness over the course of the follow-up.

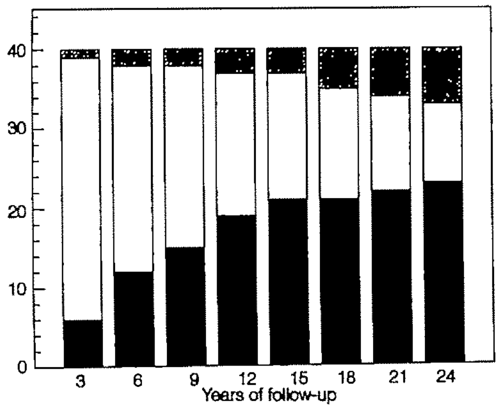

Fig. 2 Number of patients who 'recovered' (good or intermediate outcome; ■), remained ill (□) or died (▩) over the follow-up period.

Discussion

The main results of the present study can be summarised as follows. The findings at the 20-year follow-up are on the whole less favourable than those anticipated at the five-year follow-up. In particular the deaths attributable to anorexia nervosa rose to 15% by the end of the 20 years. The predictors of outcome in the earlier study remained broadly valid in determining the 20-year outcome: a later age of onset in particular was predictive of a worse outcome. Individual patients could still recover even after being ill for over 15 years, but the rate of recovery decreased sharply after a duration of 12–15 years. At least 15% of the patients progressed to the full syndrome of bulimia nervosa.

There are two important qualifications to this study. First, the findings are not automatically applicable to other series of patients recruited from different populations. A high proportion of our patients had already failed to respond to previous treatments provided by psychiatrists in other hospitals. In contrast, the series of patients followed up by Morgan *et al* (1983) had a much higher rate of 'good outcomes' than our own series (58% v. 30%). This difference is almost certainly due to the initial patient selection, as the patients studied by Morgan *et al* came originally from the clinic's neighbouring population in Bristol.

The second important qualification is that we have been obliged to ignore any long-term effects of treatment provided, especially during the first few years of the illness. It could be argued, however, that in earlier years no effective long-term treatments for anorexia nervosa had been discovered (Russell, 1977). Although our patients had initially received vigorous in-patient treatment which had succeeded in achieving weight gains, no long-term treatment had been provided. For example, family therapy, recently shown to improve the one-year outcome in younger patients (Russell *et al*, 1987), was not available in the 1960s when the patients were originally treated. On the whole, therefore, it is reasonable to discount possible long-term effects of treatment in an old series of patients as reported here.

This study highlights the serious nature of anorexia nervosa when it takes a chronic course. After 20 years, almost 40% of the patients were still gravely incapacitated by the illness or had died. The high mortality rate is similar to the 18% reported by Theander (1985) and a little lower than that of the series of Halmi *et al* (1975). Perhaps even more striking is the high level of dysfunction in other areas of life. Of those still alive at follow-up, one third led a socially isolated and restricted life, and reported a high dependence on their families of origin. Attitudes to sexuality, marriage and child-bearing were still problematic for at least half the patients.

Compared with the results of shorter-term follow-up studies (Theander, 1970; Morgan & Russell, 1975; Hsu *et al*, 1979) the number of patients with normal body weights was low, with a trend towards a lowering of body weight in the group as a whole. It is arguable that this is not necessarily crucial, as five patients whose weight was moderately low menstruated regularly and were well in all other respects. The prevalence of dietary restriction and preoccupation with thoughts of weight, food or appearance was slightly lower than in the earlier follow-up.

Against these rather bleak facts one has to set the finding that a possibility of recovery remains even after a very prolonged illness. It is true that with increasing length of illness the probability of recovery is gradually reduced and diminishes sharply after 12–15 years. Nevertheless, even after being ill for 15 years or more some patients still recovered. This finding contrasts with the views expressed in recent review articles (Hsu, 1980; Schwartz & Thompson, 1981; Steinhausen & Glanville, 1983) and with Dally's (1969) assertion that recovery is not possible after seven years. Our finding is supported by Theander's (1985) study.

Comparisons with the earlier follow-up study (Morgan & Russell, 1975) are of interest because they highlight the overall course of the illness and throw light on the reliability of the outcome measures used. Although there was a fair degree of consistency in outcome for the group as a whole between the two follow-ups, a number of individuals changed considerably. The majority of those who had a poor outcome at five years were still doing badly after 20 years, but approximately one third were improving. Conversely, of those in the intermediate or good outcome category, just over one fifth relapsed and had a poor outcome at 20 years. This is a more serious form of prognostic error, and is highlighted by the three deaths among the patients judged to be in the 'good' or 'intermediate' outcome categories at the five-year follow-up.

The distinction between good and intermediate outcome is less clear-cut. The finding that the clinical ratings of the patients in the intermediate and good outcome groups were very similar suggests that the classification of intermediate outcome does not so much signify a worse outcome but rather our uncertainty in assessing the patient. The categories of outcome that we used are based on weight and menstrual function. Where both are normal or both clearly abnormal there is little problem in rating outcome. Where one or both are marginal, classification is more problematic. Taking into account the patients' level of functioning over an extended period of time we were able to conclude that a third of the patients in the intermediate outcome group were functioning well in spite of their relatively low weight. This finding, in conjunction with the low correlation between the patients' weights at five years and 20 years, suggests that weight is less reliable as an indicator of long-term compared with short-term outcome.

The other difficulty in the classification of outcome arose from the need to use two somewhat different sets of criteria. Since the description of bulimia nervosa as a variant of anorexia nervosa (Russell, 1979) only occurred after the completion of the first follow-up study, bulimic symptoms could obviously not be included in the criteria for the overall outcome at that time. In view of current knowledge, it was necessary to include these symptoms in the classification of outcome at 20-year follow-up. This addition precludes, however, a comparison between the earlier and current follow-up studies. The compromise of using a dual classification allowed us to make this comparison as well as take into account those patients who developed bulimia nervosa.

Before discussing the different prognostic factors it is important to stress the need for caution in drawing general conclusions on the basis of a necessarily unrepresentative sample of the general population of eating-disordered patients.

One further limitation needs to be mentioned: our data, as in other research of this kind, were in part derived from a retrospective case-note study. Hsu (1980), Schwartz & Thompson (1981), Garfinkel & Garner (1982) and Steinhausen & Glanville (1983) have commented on the problems of this method and we are aware that this is a possible source of contamination. This reservation applies in particular to the data concerning pre-morbid adjustment and family relationships. Other data such as age of onset or length of illness are less likely to be affected.

Nevertheless, this study confirms in a number of aspects the findings of the earlier Maudsley study and the work of other authors. The variables that predicted outcome at five years, in the main, remained good predictors of the long-term outcome at 20 years. The strongest of these predictors is the age of onset of the illness, and this finding is consistent with those of most studies. There is, however, some dispute whether a very early age of onset is necessarily associated with a good outcome. Swift (1982) has argued that the evidence for an onset before the age of 15 years as an indicator of a good prognosis is inconclusive and Bryant-Waugh *et al* (1988) suggest that a pre-pubertal onset is in fact associated with a poor prognosis. In our sample the most favourable outcome was among the patients whose illness started between 11 and 15 years. It has to be said, however, that only two of our patients became ill before their menarche. A poor pre-morbid individual adjustment and in particular a history of disturbed relationships in the family were also found to be associated with a poor outcome.

The relationship between the length of illness on admission and outcome is more difficult to interpret. For many of the patients the original admission to the Maudsley hospital was just one in a series of many admissions. Relating outcome to variables associated with this particular admission is in some ways arbitrary. The relationship between the length of illness and eventual outcome as shown by Fig. 1, however, remains strong and confirms the findings of other long-term follow-up studies (Theander, 1985; Isager *et al*, 1985).

The conclusions from this study are clear. The natural course of anorexia nervosa can be ominous, especially with a later age of onset, leading to chronic disability or even death. Accordingly, it is essential to develop treatments which are likely to improve the eventual outcome (Russell *et al*, 1987). Moreover, we have shown that patients can recover even after several years of illness, so that it is never too late to attempt a vigorous programme of treatment.

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†We announce with regret the death of Dr Harsha Ratnasuriya on the 24th February 1989, after he had completed the patient follow-up.

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The Effects of Clozapine on Tardive Dyskinesia

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This article reviews eight published studies that describe clozapine's effects on TD and examines the outcome of 30 patients with TD treated with clozapine for up to 36 months. These data indicate that TD response to clozapine is variable but that approximately 43% of cases, particularly those with dystonic features, improved after clozapine treatment. Methodological limitations of the studies described, however, preclude definitive conclusions, which must await appropriately controlled trials.

First identified nearly three decades ago, tardive dyskinesia (TD) remains a significant public health problem and a serious limitation of neuroleptic drug treatment. An average TD prevalence rate among neuroleptic users of 20% has been reported, but this varies widely in different patient populations, reflecting varying levels of vulnerability and treatment practices (Kane & Smith, 1982). A prospective study of 800 patients indicated an incidence of new cases of 5% with each year of neuroleptic exposure, but also a spontaneous remission rate of 32% in the subsequent year, even with continued treatment; this annual incidence rate remained fairly stable over eight years of exposure, while the remission rate declined gradually (Kane *et al*, 1986). Although the risk of TD may seem alarming, the majority of patients who develop the disorder have mild, non-distressing symptoms which do not impair functioning.

A minority of neuroleptic-treated patients develop severe symptoms of TD which are markedly distressing and disabling. These symptoms may include dyskinetic variants of the classic choreoathetoid movements of TD such as dystonia (Burke *et al*, 1982) and akathisia (Barnes & Braude, 1985). Moreover, TD may even be life-threatening owing to such complications as dysphagia, respiratory disturbance, and renal failure from dehydration or rhabdomyolysis caused by muscle breakdown from increased motor activity (Yassa & Jones, 1985; McClelland *et al*, 1986; Youssef & Waddington, 1987). Severe TD sometimes is persistent even after neuroleptic medication is withdrawn (Burke *et al*, 1982). Although drug withdrawal should be considered as a course of action when TD, particularly severe TD, develops, this is often not feasible because of the risk of psychotic relapse.

All current neuroleptics approved by the US Food and Drug Administration have been associated with the development of TD, although whether the liability of all drugs to produce TD is similar is undetermined (Baldessarini *et al*, 1980). One possible exception is the atypical antipsychotic agent clozapine. Clozapine, a dibenzodiazepine (8-chloro-II [4-methyl-1-piperazinyl]-5H-dibenzo[b,e] [1,4]diazepine) differs from classic neuroleptics (Schmutz & Eichenberger, 1982) in that it does not induce catalepsy (Burki *et al*, 1975) or block stereotypies induced by dopamine (DA) agonists, (Ljungberg & Ungerstedt, 1978), or, after chronic treatment, produce DA receptor supersensitivity (Sayers *et al*, 1975), or produce a depolarisation state (Chiodo & Bunney, 1983) in the A-9 nigrostriatal dopamine neurones of rodent brain. Clinical studies have demonstrated that clozapine rarely, if ever, causes Parkinsonism, dystonia or TD, nor does it elevate levels of prolactin (Lieberman *et al*, 1986, 1989*a*). At the same time the compound has antipsychotic activity and has been shown to be effective in some patients refractory or intolerant to standard antipsychotic treatment (Juul Povisen *et al*, 1985; Kane *et al*, 1988). A recent multicentre study found that clozapine was superior in antipsychotic efficacy to standard neuroleptic treatment with haloperidol or chlorpromazine and that approximately 30% of patients whose psychotic symptoms were classified as refractory improved with clozapine (Kane *et al*, 1988).

Some investigators have suggested that, in addition to lacking the capacity to induce TD, clozapine may have therapeutic effects in TD (Cole *et al*, 1980; Gerbino *et al*, 1980), but published reports examining clozapine's action on cases of neuroleptic-associated TD are limited by methodological problems and vary markedly in their findings (see literature review below). If clozapine has therapeutic potential in TD, this would be of great significance, as no satisfactory treatment currently exists; clozapine may thus permit treatment of TD with psychoses, and may yield information about the pathophysiology of TD.

The purpose of this paper is to review the literature on clozapine's effects on TD and describe our experience at the Hillside Hospital with clozapine in TD.

Literature review

We found eight studies in which clozapine's effects on TD were described (Gerlach *et al*, 1974; Carroll *et al*, 1977; Simpson *et al*, 1978; Caine *et al*, 1979; Cole *et al*, 1980; Gerbino *et al*, 1980; Meltzer & Luchins, 1984; Small *et al*, 1987).

Gerlach *et al* (1974) compared the therapeutic efficacy of clozapine and haloperidol against TD in a small, controlled double-blind cross-over study. Following a three-week drug-free interval, four patients received haloperidol and four clozapine for three weeks and then, after a second three-week wash-out, received the other treatment for three weeks. Daily oral dosage was increased to 9 mg haloperidol or 225 mg clozapine. Information about rate of dose increase and time on maximum dosage was not provided. TD symptoms decreased in five of the eight patients and increased in one on haloperidol but returned to baseline severity following withdrawal of this drug. The authors observed clozapine to have no definite effect on TD symptoms, and noted that TD decreased slightly in two patients following withdrawal of this drug. This study suffers from the short period of active treatment and the relatively low dose of the agents tested. Because clozapine treatment typically is initiated at low doses and is increased gradually (Small *et al*, 1987; Lieberman *et al*, 1989*a*), it is unlikely that daily doses at 200 mg or more were used for much longer than a week. The study primarily demonstrates that clozapine at doses up to 225 mg daily failed to suppress TD within three weeks, although, as repeatedly reported by others (Jeste & Wyatt, 1982), a moderate dose of haloperidol was effective.

Carroll *et al* (1977) treated one patient with a severe neuroleptic-associated movement disorder that included both choreoathetoid and dystonic elements, with serial trials of different agents including clozapine (up to 1000 mg daily) for 18 days. Clozapine produced a "significant effect" on the patient's TD; symptoms returned following drug withdrawal.

Simpson *et al* (1978) studied seven patients (aged 35–64 years, mean age 50) with moderately severe TD involving orofacial areas and extremities, in a single-blind, placebo-controlled, double cross-over design (two weeks of placebo, 18 weeks of clozapine, 12 weeks of placebo). Patients received mean daily doses of 523–775 mg for the last four weeks of clozapine treatment. TD symptoms showed marked variability but tended to improve in the last weeks of the 18-week clozapine phase of the trial. The mean total rating scores on the Abnormal Involuntary Movement Scale (AIMS) for the sample fell from 26 at the initial phase to 12 at the end of the clozapine phase. Five of ten symptom item AIMS scores were significantly lowered by clozapine. However, TD symptoms reverted to their baseline severity during the second placebo period after discontinuation of clozapine. The authors concluded that the overall anti-TD effect was only moderate.

Caine *et al* (1979) performed a double-blind placebo-controlled cross-over study with clozapine in a heterogeneous group of patients with movement disorders: four patients with Tourette's syndrome, three patients with Huntington's disease and two psychotic patients with TD with dystonic features. Each treatment period lasted four to seven weeks with three to five weeks at maximum doses. One Tourette's patient showed a decrease in motor tics by over 50% on the AIMS rating, although there were no changes in behavioural symptoms. The two patients with Huntington's disease were improved on clozapine and one had a dramatic worsening when the drug was withdrawn. The authors report that the symptoms of the Tourette's and Huntington's patients showed greater improvement in subsequent treatment with haloperidol. The two TD patients showed no benefit from clozapine. Although well controlled, this study is limited by the low doses used (the TD patients' mean (s.d.) daily dose of clozapine was 363 (63) mg) and the small and heterogeneous patient sample.

Cole *et al* (1980) described the open, uncontrolled treatment of 27 TD patients given clozapine at doses adjusted to treat the patients' psychiatric symptoms. Twenty-one patients received 100–300 mg and six received 500 mg or more daily. The authors report that the drug "had a mild to moderate effect in reducing dyskinesia", and that no case of TD worsened. The greatest improvement occurred in 12 patients who were treated with clozapine for 12 weeks or more; two of these showed complete remission, one had marked improvement.

Gerbino *et al* (1980) treated 24 patients (15 men, 9 women, aged 19–64 years) with clozapine in an open trial for a minimum of four weeks and then followed 17 of these for a year of maintenance treatment. In addition to having TD, most patients had been unresponsive to conventional antipsychotic treatment. Two patients received daily doses of clozapine of over 900 mg, but the average daily dose during the acute treatment phase of the study was 650 mg. By the end of the clozapine trial, all 24 patients showed at least 50% reduction in severity of the symptoms of TD as rated by the AIMS (7 patients had achieved 100% remission, 1 90%, 11 75%, and 5 50%). In addition, the authors reported that another six patients who had dropped out during the acute treatment phase also had shown about 75% reduction in AIMS scores. Fourteen of the 24 patients later had their dose of clozapine reduced by 50% and continued to show an average of 90% improvement in TD symptoms. Three patients were withdrawn from clozapine after a year and still maintained a 95–100% improvement in TD.

These follow-up data are crucial to the determination of whether clozapine masks TD, as do other neuroleptics, or actually has therapeutic effects on TD. No recurrence of TD symptoms was observed in the 17 patients followed up long-term. Moreover, no symptoms re-emerged when drug dosage was reduced or, in the three cases after one year, withdrawn. Based on these results, the authors suggested that clozapine treatment did not merely suppress TD but rather resulted in sustained improvement of TD symptoms.

Meltzer & Luchins (1984) described a dramatic therapeutic response of a 32-year-old woman with severe TD, including dystonia, to clozapine (900 mg per day): the AIMS total score declined from over 20 to 13. Since improvement was seen within two weeks, the authors concluded that clozapine was masking TD symptoms. However, this improvement was sustained through nine months of continued treatment.

Small *et al* (1987) described 19 patients with TD in a larger group studied in an open, uncontrolled trial of clozapine as an antipsychotic. Dose was adjusted by clinical response to a maximum daily dose of 340 mg per day. All patients showed improvement in TD by clinical impression during the first seven weeks of treatment. However, symptoms returned to their original severity at the end of the trial following drug withdrawal in all but one patient, a 58-year-old woman with severe TD. Seven patients evaluated with the AIMS showed a decrease in mean total scores from 20 to 4 after seven weeks of treatment. This study is limited in that only eight patients received clozapine for longer than six months and only at relatively low doses (<350 mg a day).

Interpretation of these studies is limited by several methodological problems, including the use of relatively low, possibly inadequate clozapine doses, lack of adequate controls and, most importantly, lack of consistent evaluation following withdrawal of clozapine. Despite these limitations, a number of patients, including some who were severely affected, appear to have experienced dramatic improvement in TD with clozapine. However, from the information provided there are no discernible factors that distinguished which patients were responsive to clozapine.

To examine further the effects of clozapine on TD, we evaluated the response of 30 patients with TD who were treated with clozapine at Hillside Hospital.

Method

Patients were referred to our clozapine programme because of treatment resistance or intolerance to standard antipsychotic pharmacotherapy. Treatment resistance was defined as the persistence of positive psychotic symptoms of at least moderate severity, despite separate trials with three different neuroleptics of two or three chemical classes in daily oral doses greater than the equivalent of 1000 mg chlorpromazine a day for at least six weeks. Treatment intolerance was defined as the presence of severe TD or the occurrence of severe acute extrapyramidal side-effects of standard doses of neuroleptic drugs. In addition, patients had to meet the following criteria: (a) age 18–40 years; (b) presence of a primary psychiatric disorder (axis I, DSM–III) (American Psychiatric Association, 1980) for which antipsychotic drug treatment is indicated for more than six months, uncomplicated by substance abuse; (c) no current or past history of serious medical illness, particularly idiopathic or drug-induced blood dyscrasia. In addition, patients and their families, after being appraised of the potential risks and benefits of clozapine treatment, were required to give informed consent.

Patients were admitted to our in-patient service and withdrawn from medication for two to four weeks depending on their behavioural status in the drug-free period. They were examined for TD at one and two weeks after drug withdrawal and on two separate days in the week before starting clozapine. The final TD examination was used for the baseline evaluation unless it did not agree with the preceding examination. In such cases the mean of the last two ratings was used. These TD examinations consisted of an assessment, lasting five to ten minutes, using the Hillside version of the Simpson Dyskinesia Scale (SDS; Lieberman *et al*, 1984). This scale comprises 28 symptom items and a global score. In addition, seven body-area global items (face, lips, jaw, tongue, upper extremities, neck and trunk, lower extremities) that correspond to AIMS items are included. All 36 items are rated on a six-point severity scale (0 = none, 1 = questionable, 2 = mild, 3 = moderate, 4 = moderately severe, 5 = very severe).

Following baseline evaluation, clozapine was started gradually on a twice-daily schedule, with dose increased as tolerated to 500 mg a day by day 21 and held at maximum dose for at least one week. Subsequently, dose was adjusted as clinically indicated, to a maximum of 900 mg a day.

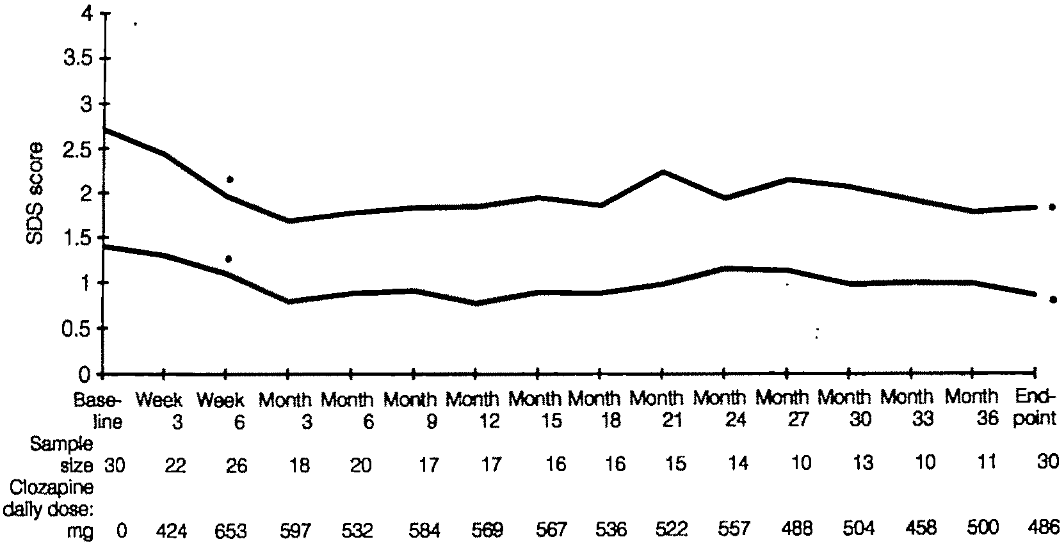

Fig. 1 The SDS scores for overall global item (upper line) and the seven body-area global items (lower line) for the sample displayed over the period of time on clozapine (number of patients and mean dose are shown below). End-point reflects the last rating of patients whenever it occurred (mean (s.d.) end-point = 27.8 (18.2) months). The apparent increase in symptoms at months 21 and 24 are artefacts of the diminishing number of subjects rated at those time points. End-point analyses of SDS ($n = 15$ and 14 subjects respectively) showed significant reductions in SDS scores and were consistent with those of the entire sample (mean (s.d.) change in body global scores = 0.58 (0.52), $t = 5.67$, d.f. = 25, $P < 0.001$; mean (s.d.) change in overall global score = 1.0 (0.94), $t = 6.03$, d.f. = 28, $P < 0.001$) ($^*P < 0.001$).

Dose adjustments were aimed at optimising treatment so as to alleviate psychopathology, with tolerable side-effects. After six weeks of treatment a judgement was made as to whether the patient had responded sufficiently to warrant continued treatment with clozapine. Patients who had shown sufficient improvement were discharged and followed as out-patients on clozapine. TD evaluations were performed at 12-week intervals. During this follow-up period the dose of clozapine was adjusted on a clinical basis to a lower but effective dose.

Results

Fifty-eight patients began this clozapine protocol. Twenty-one discontinued or were withdrawn from treatment for reasons of non-compliance (20%), side-effects (50%) or lack of response (30%). These cases were excluded from data analyses. Thus 37 patients received clozapine treatment for a sufficient period of time (minimum of 12 weeks) to be included in the analyses. The sample had a mean (s.d.) age of 27.8 (5.8) years; 27 were men; 34 were Caucasian, 2 black and 1 Asian. According to DSM–III diagnosis, 33 had schizophrenia, 3 schizoaffective disorder and 1 bipolar major affective disorder with mood-incongruent psychotic symptoms. They had been psychiatrically ill for a mean (s.d.) of 8.8 (4.6) years and had received neuroleptic treatment for a mean (s.d.) of 5.8 (3.7) years. Twenty-four were given clozapine because of treatment resistance, and 13 because of treatment intolerance. The 37 patients reported were followed on clozapine for a mean (s.d.) of 25.7 (18.1) months (range 3–66 months). In addition to clozapine, 18 patients concomitantly received other medications for varying times, including atenolol (25–50 mg a day), phenobarbitol (45 mg a day), alprazolam (1–2.5 mg a day), lorazepam (0.5–4.0 mg a day) and lithium (600–900 mg a day).

Before starting clozapine, 30 had TD. Of the seven patients without TD, none developed it during a mean (s.d.) of 16.9 (16.0) months of clozapine treatment. There was no significant increase in the SDS ratings (mean of seven body-area global items) from baseline to the follow-up end-point for the seven non-TD patients (mean (s.d.) change score = 0.08 (0.32), $t = 0.68$, 0.68, d.f. = 6, NS).

Among the 30 patients with TD, its severity ranged from mild to severe, with a mean (s.d.) group SDS overall global rating of 2.7 (0.9) out of a maximum possible score of five. All patients had several body areas involved and seven had significant dystonia that would meet the criteria of Burke *et al* (1982) for tardive dystonia. The mean group TD scores declined slightly but significantly in the initial 12 weeks of clozapine treatment but showed no statistically or clinically significant further improvement or worsening in SDS scores over the additional 33-month follow-up (Fig. 1). An end-point analysis of SDS scores after a mean (s.d.) of 27.8 (18.2) months of treatment indicated that, compared with the baseline severity, the group maintained a mean 38% reduction in TD symptoms. By comparing end-point and baseline ratings of the entire sample, 16 patients (43%) had a decrease in TD severity (reflected by the seven body-area global items) of 50% or more. This improvement in TD symptoms was clinically as well as statistically significant.

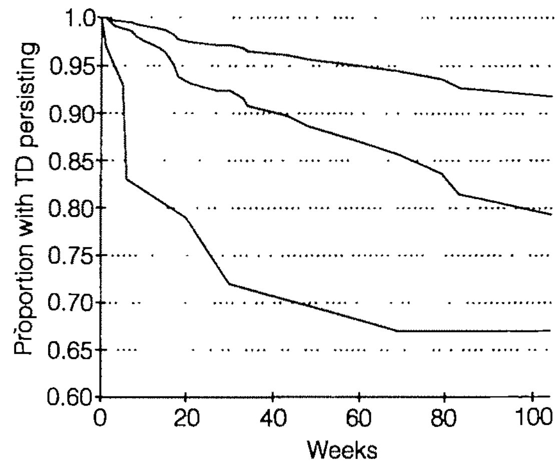

Fig. 2 The proportion of patients with TD in three treatment groups (clozapine (bottom line), CPZE 1000 mg a day (middle line), CPZE 1800 mg a day (top line)) (data for latter two groups from Kane *et al* (1986)) whose TD symptoms remitted. Remission was defined as a global rating of 0 (absent) or 1 (questionable) on the modified SDS. Remission rates for specific doses of standard neuroleptics are projected by means of the Cox proportional-hazards algorithm, based on a sample of 95 cases in which the daily dosage ranged from 200 to 2000 mg CPZE. The remission rate for the clozapine patients is the observed rate for a sample of 30 cases in which the clozapine daily dose ranged from 500 to 900 mg (1000–1800 mg CPZE).

To examine TD response another way, the proportion of patients in whom TD remitted while receiving clozapine was determined. Remission was defined as a global rating of 0 (absent) or 1 (questionable) which persisted for 12 weeks. As shown in Fig. 2, the remission rate for clozapine-treated patients was 31% in the first year and 34% by two years. This rate compares favourably with the spontaneous remission rate observed in a prospective TD study ongoing in this institution since 1979 (Kane *et al*, 1986). In this study, 95 patients who had developed TD while being treated on a clinical basis with various neuroleptics in daily doses which ranged from 200 mg to 2000 mg chlorpromazine equivalents (CPZE) were seen at regular intervals. The demographic and clinical features of this sample are as follows: they were 30.3 (10.8) years of age, 51% male and had the following psychiatric diagnoses: affective disorder 14%, schizoaffective disorder 18%, paranoid schizophrenia 17%, other axis I disorders 28%; they had been psychiatrically ill for only 6.5 (4.5) years. When we look at remission of TD symptoms, a total of 23% (95% confidence interval ± 10%) of all 95 patients remitted over the first year and 33% (± 13%) within the first two years.

It is important to note, however, that the modal dose of neuroleptics following development of TD proved to be a critical factor in the likelihood of remission, with patients on a low modal dose (the range was 0–2000 mg a day CPZE) more likely to remit ($\chi^2 = 6.79$, d.f. = 1, $P = 0.009$). Thus, the appropriate comparison group for the clozapine sample is not the entire patient sample, but rather those patients whose daily neuroleptic dosage was in the range of 1000–1800 mg CPZE (corresponding to a daily clozapine dosage of 500–900 mg). The remission rates for these groups were projected by means of the Cox proportional-hazards algorithms to be (for 1000 mg a day CPZE) 12% at one year and 21% at two years; or (for 1800 mg a day CPZE) 5% at one year and 8% at two years (Fig. 2).

This comparison group differs from the clozapine group on a number of factors which were found to affect the likelihood of remission. Specifically, in the clozapine group, the TD tended to be much more severe and of substantially longer prior duration. Additionally, the criterion for remission used in the clozapine study was more stringent. The fact that the remission rate for clozapine, controlling only for modal dose, is still substantially higher than the rate observed for the comparison group, suggests strongly that clozapine does increase the probability of TD remission beyond the observed rates of spontaneous remission.

The TD response of individual patients was markedly variable: some patients improved while others showed no change. The average daily doses at week six and the end-point were 653 and 486 mg, respectively. Although there was some variation in the doses of clozapine given over time, generally reductions, variability in TD response was not related to dose differences between or within patients. To the extent that any relationship between TD response and clozapine dose was apparent, higher dosage was associated with greater improvement in TD ($r = -0.21$, NS). The most substantial reductions in TD symptoms occurred in the four patients with tardive dystonia. This is illustrated in Fig. 3, which shows separately the body-area global ratings for the head and neck regions (where dystonic pathology was concentrated) and the mean of the six other body areas (face, lips, jaw, tongue, upper and lower extremities) and the overall global rating of four patients. Fig. 3(a) is for a 24-year-old man whose severe truncal and neck dystonia was suppressed during the first two weeks of clozapine treatment but fully returned when medication was withdrawn. Fig 3(b) is for a 20-year-old man followed on clozapine for almost two years whose truncal and neck dystonia declined and ultimately fully subsided on clozapine treatment, while choreoathetoid movements in other body areas persisted after gradual decline. Since medication was not discontinued it is not known if the dystonia resolved or merely was suppressed. Fig. 3(c) is for a 27-year-old woman whose TD (dystonia and choreoathetoid symptoms) subsided with clozapine treatment. This improvement persisted for 20 days after clozapine was stopped, but then the dystonia began to recur when the patient was treated with haloperidol due to psychotic relapse. The dystonia eventually was suppressed by continued administration of an increased dose of haloperidol. Fig. 3(d) is for a 38-year-old man whose TD initially declined with clozapine treatment, in a dose-dependent manner. His non-neck and trunk choreoathetoid symptoms returned whereas the dystonia continued to subside and remained so even when the clozapine was stopped after 14 months of treatment.

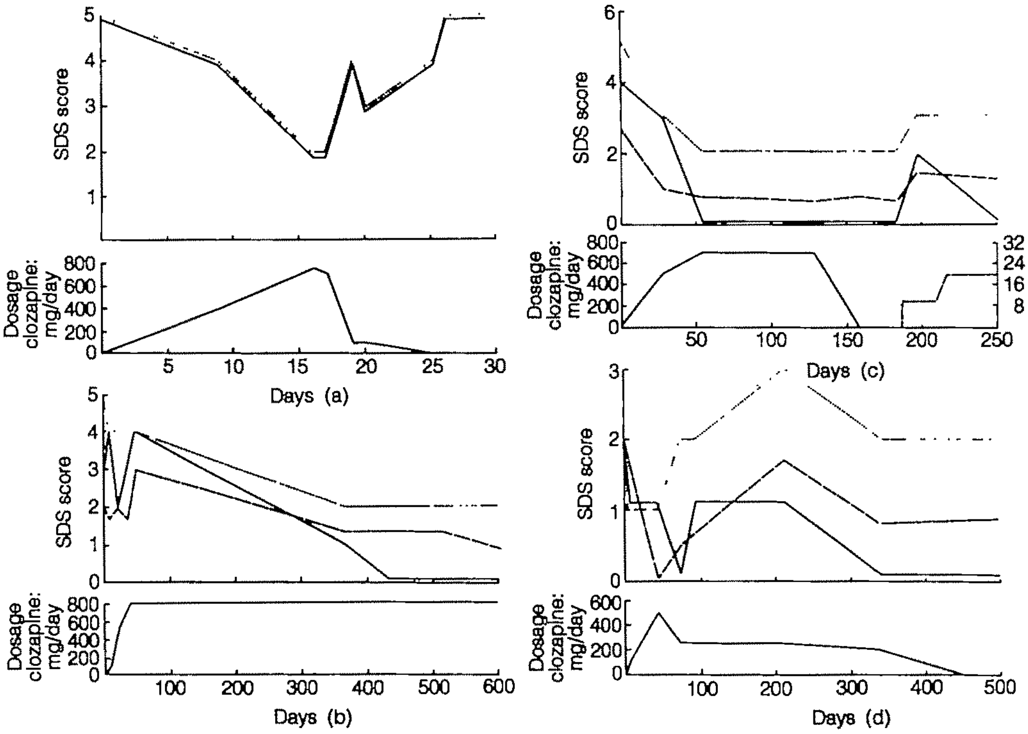

Fig. 3 The TD response of two patients treated with clozapine as reflected by three different measures from the modified SDS: the item for neck and trunk body areas (———); the mean of six body-area items (face, lips, tongue, jaw, upper and lower extremities) (—); and the overall global item (······). The drug dose is shown in mg per day for each patient below their TD reponse. (a) The patient is a 24-year-old man with severe truncal dystonia. Only his dystonia was rated. (b) A 20-year-old man with truncal dystonia and choreoathetoid movements of the orofacial areas and upper extremities. (c) A 27-year-old woman with truncal and facial dystonia and choreoathetoid symptoms of the upper and lower extremities. (d) A 38-year-old man with torticollis and choreoathetoid movements of the face and upper and lower extremities.

Discussion

These results, along with the previously published studies reviewed, indicate that clozapine has an apparent beneficial effect (50% or greater reduction) on TD symptoms in approximately 43% of patients with pre-existing TD. The therapeutic effects appear to be greatest in cases of severe TD, particularly tardive dystonia, and less prominent although apparent in some patients with typical choreoathetoid symptoms. Any interpretation of these results, however, must be tentative, because of the methodological limitations of the available studies. Ideally, to evaluate clozapine's efficacy in TD, studies should include random assignment of patients to clozapine and a comparison treatment condition, assessment of treatment response under double-blind conditions, and systematic drug-withdrawal periods to determine whether symptoms were being suppressed or permanently alleviated.

However, in lieu of this and on the basis of current evidence, we must consider the different mechanisms by which clozapine could have apparent therapeutic effects in TD. Symptoms of TD could be suppressed by clozapine as by classic neuroleptics. The decrease in TD symptoms in the acute treatment period is consistent with this. The fact that TD symptoms do not re-emerge over follow-up, however, mitigates against this explanation. Following the initial suppression of TD symptoms when standard neuroleptic treatment is instituted, symptoms could be expected to re-emerge gradually, and eventually approach their baseline level of severity. At the same time sustained treatment with classic neuroleptics would decrease the potential for spontaneous reversibility of TD symptoms (Kane *et al*, 1986).

A second explanation is that clozapine neither improves nor worsens TD directly but that the passage of time in the absence of a TD-inducing agent results in a decrease of symptoms, that is, patients with reversible TD spontaneously improve on clozapine in the absence of a classic neuroleptic. This explanation describes what might be called a 'passive' therapeutic effect. However, this explanation, although plausible, is diminished in likelihood by the fact that most of the patients had long-standing and many severe TD.

The third alternative is that clozapine's pharmacological properties have an 'active' therapeutic effect. In this case we might expect to see TD symptoms decrease in a dose-dependent and time-dependent fashion, that is, a minimum dose and duration of treatment are required for a therapeutic response. To an extent, this is seen in the reports of Gerbino *et al* (1980) and Cole *et al* (1980) as well as in our data, and is particularly illustrated by the dystonia cases. In Fig. 3(b), the patient's symptoms remained improved without recurrence while on clozapine for almost two years. In Fig. 3(a), the patient's dystonia was suppressed but then returned when clozapine was stopped after almost three weeks of treatment, while in Fig. 3(c) the patient's dystonia was suppressed and then did not return upon clozapine withdrawal at 155 days. In Fig. 3(d) the patient's symptoms subsided and did not recur even when clozapine was stopped after almost one and a half years of treatment.

From our data and those previously reported, it appears that only some patients with TD may benefit from clozapine. This is not surprising given the probable heterogeneity of TD. If clozapine acts through the 'passive' therapeutic mechanism, then only those patients with reversible TD would show improvement. However, this does not explain the relatively rapid improvement of patients with severe, long-standing and presumably irreversible, TD. A more likely explanation is that TD responds to clozapine, as with most drugs used to treat TD, in a heterogeneous fashion (Jeste & Wyatt, 1982; Lieberman *et al*, 1988). Patients with tardive dystonia in particular improved with clozapine. This subtype of TD has previously been reported to have a pharmacological profile that is distinct from more common choreoathetoid forms of TD (Burke *et al*, 1982; Lieberman *et al*, 1988, 1989*b*). Thus, tardive dystonia might selectively respond to clozapine despite being a persistent condition, while the classic choreoathetoid form of TD would improve with clozapine only if it was of a spontaneously reversible type. This difference in mechanisms could account for some of the variability in treatment response.

It is not clear what pharmacological mechanisms might mediate clozapine's putative effects on TD. Clozapine's relatively weak effects on striatal D_2 receptors (Rupniak *et al*, 1985), while consistent with its lack of acute extrapyramidal side-effects and capacity to cause TD, does not explain the apparent rapid suppression of TD symptoms in some treated patients. Clozapine also has been reported to have somewhat greater affinity to D_1 receptors relative to its D_2 binding potency that most classic neuroleptics (Arnt & Hyttel, 1984; Anderson & Braestrup, 1986). The significance of these findings is, however, unclear, as the functional role of D_1 receptors in TD pathophysiology has yet to be elucidated (Rosengarten *et al*, 1986).

Clozapine has potent anticholinergic properties which could be expected to exacerbate TD symptoms in some patients. Others, particularly those with tardive dystonia, have been shown to be responsive to high-dose anticholinergic treatment (Burke *et al*, 1982). Clozapine has effects on other neurotransmitter systems including serotonin (Reynolds *et al*, 1983) and norepinephrine (McMillen & Shore, 1978). However, it is not obvious how these pharmacological properties might account for the drug's effects on TD. Thus, as with its unique antipsychotic activity, the mechanism of clozapine's effects on TD is somewhat of a mystery which requires further investigation.

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A Double-Blind Comparison of the Effects of Gradual Withdrawal of Lorazepam, Diazepam and Bromazepam in Benzodiazepine Dependence

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Using a double-blind procedure, 68 patients with putative benzodiazepine dependence were randomly allocated to one of three groups given lorazepam ($n=22$), diazepam ($n=23$) or bromazepam ($n=23$) in doses equivalent to those of the patients' original benzodiazepine. After four weeks the dosage was reduced in 25% quantities until no further benzodiazepines were taken. A total of 23 patients dropped out during the study, ten on lorazepam (one of whom committed suicide), seven on diazepam and six on bromazepam. There were few differences in withdrawal symptoms between the three groups but, despite the higher drop-out rate, these symptoms were somewhat less marked in the lorazepam group. Withdrawal symptoms were greater in patients who had taken a benzodiazepine for >5 years and were most marked in those with personality disorders, predominantly dependent ones.

Despite much better awareness of the problems of dependence on benzodiazepines in recent years (Petursson & Lader, 1981; Higgitt *et al*, 1985; Tyrer & Murphy, 1987; Priest & Montgomery, 1988) it is still difficult to predict dependence in an individual case. Because of the absence of good predictors it is now recommended that in antianxiety treatment benzodiazepines should not be prescribed for longer than one month (Priest & Montgomery, 1988). Nevertheless, a significant proportion of patients prescribed benzodiazepines, probably a majority (Tyrer, 1988), have no problems in stopping the medication after both short- and long-term treatment, so it would be of great help to the clinician to identify the key factors that predispose to dependence.

There are several predisposing influences that are said to adumbrate pharmacological dependence. These include dosage of benzodiazepine (higher dosage carrying greater risk) (Ayd, 1979), longer duration of treatment (Tyrer, 1978; Rickels *et al*, 1983), personality status of patient (with dependent personalities most at risk) (Clift, 1972; Tyrer *et al*, 1983), and nature of benzodiazepine, with benzodiazepines of short elimination half-life and high potency (e.g. triazolam, lorazepam, alprazolam) attracting most concern (Tyrer *et al*, 1981; Griffiths *et al*, 1985; Pecknold *et al*, 1988).

However, the evidence for each of these claims is relatively slight, partly because there have been few studies that have studied sufficient patients to investigate these hypotheses adequately and also because of inherent difficulties in determining withdrawal symptoms. There have also been no studies in which the withdrawal effects of different benzodiazepines have been compared satisfactorily under double-blind conditions. We therefore carried out a study in which patients who had taken prescribed benzodiazepines regularly for six months or more and had apparent withdrawal symptoms on reduction (i.e. had putative dependence) were assigned at random to one of three different benzodiazepines and then withdrawn using a double-blind procedure. Personality status was determined before withdrawal, and in addition to other assessments a new scale was used to detect withdrawal symptoms.

Method

All patients presenting to PT's out-patient clinics between November 1985 and January 1988 were considered for the study if they:

(a) had taken a prescribed benzodiazepine in regular dosage for six months or longer
(b) were unable to reduce or stop their drug because of apparent withdrawal symptoms
(c) were taking no other psychotropic drugs
(d) were taking their benzodiazepine in a daily dosage of 2–16 mg of diazepam (or equivalent dosage of another benzodiazepine)
(e) were taking their drugs for anxiety or insomnia or related neurotic symptomatology
(f) wished to stop their benzodiazepines and were willing to take part in the study as out-patients.

Patients included in the study changed to one of three different benzodiazepines in roughly equipotent dosage to that of their original benzodiazepine (equivalent dosages used for 5 mg of diazepam were lorazepam (1 mg), nitrazepam (3.5 mg), chlordiazepoxide (10 mg), temazepam (10 mg), triazolam (0.1 mg), flurazepam (10 mg) and clorazepate (5 mg)). Using double-blind procedure the change was made to the appropriate number of tablets, each containing either diazepam (5 mg), bromazepam (3 mg) or lorazepam (1 mg). Each patient remained on this dosage until the end of the fourth week, after which the dosage was reduced in 25% aliquots at two-week intervals until complete withdrawal by the end of the tenth week. Because we were interested in the time course of withdrawal symptoms from benzodiazepines of different half-lives it was felt important to follow the withdrawal program strictly. If patients were unable to reduce their drugs at the appropriate time they were regarded as drop-outs for the purposes of the study.

On entry to the study patients had their psychiatric symptoms assessed using the Comprehensive Psychopathological Rating Scale (CPRS; Asberg *et al*, 1978), together with the Brief Scale for Anxiety (BAS) which scores the items of the CRPS commonly associated with anxiety diagnoses (Tyrer *et al*, 1984). Pre-morbid personality was also assessed, preferably at an interview with an informant, using the Personality Assessment Schedule (PAS; Tyrer & Alexander, 1979; Tyrer *et al*, 1988). Withdrawal symptoms were assessed using the Benzodiazepine Withdrawal Symptom Questionnaire (BWSQ), a 20-item self-rating scale recording the severity of common withdrawal symptoms (Tyrer *et al*, 1990).

The CPRS, BAS and BWSQ were administered at two-week intervals between entry to the study and week 14, by which time patients who had withdrawn from their benzodiazepines completely would have taken no drugs for four weeks. Blood pressure, resting pulse and weight were recorded at week 4 (immediately before reduction of the allocated benzodiazepine) and at week 12, two weeks after the benzodiazepine was stopped. Venous blood samples were taken for serum benzodiazepine estimations at weeks 4 and 12 also, using a high-pressure liquid chromatography (HPLC) technique. The code was broken by a pharmacist independent of the main study in order to indicate the appropriate benzodiazepine for estimation, although if there were significant quantities of other benzodiazepines present these could also be detected.

The data were analysed mainly using repeated measures analysis of variance, although χ^2 statistics were used for categorical data.

Results

A total of 68 patients entered the study. To ensure roughly equal proportions of patients in each drug group, randomisation of patients was constrained so that there were 20 patients in each group after 60 had been allocated. Of the 68 patients, 22 were allocated to diazepam, 23 to lorazepam and 23 to bromazepam. The three groups showed no important differences in demographic characteristics (Table 1) and had taken their benzodiazepines for a mean of around eight years. A total of 22 (32%) were taking 6 mg or less of diazepam equivalents daily on entry and 14 (21%) were taking 15–16 mg equivalents, with the remaining 32 patients taking intermediate doses between 6 mg and 15 mg. All but five of the patients had received previous psychiatric treatment, 17 as in-patients. Previous benzodiazepines taken included diazepam ($n = 25$), lorazepam ($n = 19$), nitrazepam ($n = 10$), temazepam ($n = 7$), chlordiazepoxide ($n = 3$), flurazepam ($n = 2$), and triazolam and clorazepate (one each).

Forty-five patients completed the study and examination of serum benzodiazepine levels showed all had probably complied with the withdrawal regime apart from one patient allocated to bromazepam who was found to be taking diazepam at week 12 (serum diazepam 570 nmol/l; serum nordiazepam 760 nmol/l; no bromazepam detected). As there were no differences between the results of analyses when these data were not included, this violation of the study protocol had no important influence on the findings. Of the 23 drop-outs 10 had been allocated to lorazepam, seven to bromazepam and six to diazepam ($\chi^2 = 1.5$; d.f. 2, NS). Only six (26%) of the 23 drop-outs were taking their benzodiazepine drug as a hypnotic compared with 19 (42%) of the 45 completers ($\chi^2 = 1.08$), NS). The drop-outs took place at irregular intervals throughout the study, with no consistent pattern being shown (Fig. 1). Most of the patients who dropped out did so because of increased symptoms (Fig. 1) which precluded further reduction at the planned time. These symptoms included repeated sensations of 'internal raining' (a form of tactile hallucination), hot 'patches' in the skin, and numbness and weakness in both arms (which disappeared when the benzodiazepine was resumed). One patient allocated to diazepam was admitted in the 13th week of the study, and another, allocated to lorazepam, committed suicide by drowning after 12 weeks' treatment.

Table 1
Basic demographic data of patients

	Diazepam ($n = 22$)	Trial drug Lorazepam ($n = 23$)	Bromazepam ($n = 23$)	Significance of difference
Mean age (s.d.): years	49.5 (12.6)	42.1 (9.1)	43.4 (12.0)	$F = 2.7$, d.f. 2, $P = 0.07$
Mean duration of treatment (range): months	90 (6–300)	103 (7–300)	83 (6–204)	$F = 0.31$, d.f. 2, NS
No. of female patients (%)	19 (86)	17 (74)	16 (70)	$\chi^2 = 1.9$, d.f. 2, NS
No. with marital status:				
single (%)	2 (9)	6 (26)	5 (22)	$\chi^2 = 5.1$, d.f. 6, NS
married (%)	11 (50)	13 (57)	12 (52)	
divorced (%)	7 (32)	4 (17)	5 (22)	
widowed (%)	2 (9)	0	1 (4)	

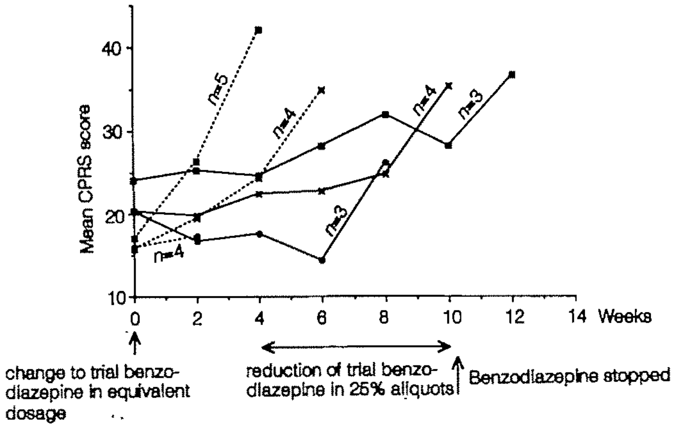

Fig. 1 Mean CPRS scores against time for patients who dropped out during the study.

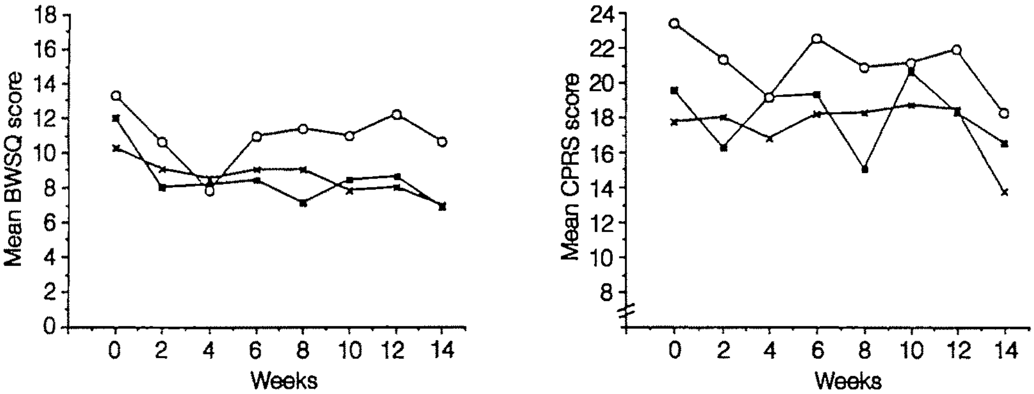

Fig. 2 Mean scores for withdrawal symptoms (BWSQ) and total psychopathology (CPRS) in 45 patients randomly allocated to lorazepam; (-■-; $n=13$), diazepam (-○-; $n=16$) and bromazepam (-+-; $n=16$) who completed the full withdrawal programme.

There were significant changes in CPRS ($F=3.3$; d.f. 7,36; $P<0.01$) over the 14 weeks of the study and in BWSQ scores between weeks 4 and 12 ($F=7.6$; d.f. 1,43; $P<0.01$). At first there was improvement (lower scores) after changing to the trial benzodiazepine followed by an increase in symptoms at variable times during the period of withdrawal between weeks 4 and 14 (Fig. 2). Anxiety scores on the BAS did not show significant changes overall with time ($F=2.0$; d.f. 7,36; $P=0.08$) although separate comparisons between baseline scores and each assessment week showed a significant difference between weeks 0 and 14 ($F=6.9$; d.f. 1,42; $P=0.012$). There were no significant changes in pulse rate, systolic or diastolic blood pressure, or weight between weeks 4 and 12 or between the drug groups. Some patients found it difficult to change over to their new benzodiazepine drug and four patients dropped out at this early stage. To determine whether the change to a different benzodiazepine affected symptoms a separate analysis was made of symptoms experienced in those patients who changed at random to the same benzodiazepine as their original drug (unchanged group) and the remainder (changed group) who transferred to a different benzodiazepine. A total of 14 of the 68 patients were in the unchanged group (eight on diazepam and six on lorazepam); these showed no significant differences in symptoms from the changed group between weeks 0 and 4 in the study (CPRS–time interaction F-ratio$=0.06$, BAS F-ratio$=0.6$, both with d.f. 2, 132 and $P>0.05$).

There were no significant differences in CPRS and BAS scores between the three drug groups, nor in total BWSQ scores or in any drug–week interactions (all F values<1). However, the scores for the diazepam group were generally higher than those for the other two drugs (Fig. 2). Two of the 20 symptoms in the BWSQ showed a significant drug–week interaction with lower scores in the lorazepam group during withdrawal (Table 2). Although these findings do not indicate a great difference between the drugs (one difference at the 5% level would be expected by chance as

Table 2
Mean scores for the BWSQ symptoms (range 0–2) of abnormal taste and feeling faint during withdrawal from diazepam ($n = 16$), lorazepam ($n = 13$) and bromazepam ($n = 16$) in 45 patients who completed withdrawal

	Abnormal taste[1]			Feeling faint[2]		
Week of study	Diazepam	Lorazepam	Bromazepam	Diazepam	Lorazepam	Bromazepam
4	0.38	0.69	0.63	0.38	0.23	0.38
6	0.56	0.62	0.44	0.63	0.00	0.31
8	0.31	0.39	0.44	0.31	0.08	0.38
10	0.44	0.38	0.56	0.44	0.08	0.19
12	0.50	0.31	0.69	0.63	0.39	0.13
14	0.50	0.15	0.56	0.44	0.23	0.19

1. F-ratio (weeks) = 1.95; d.f. 5,210; $P = 0.087$.
F-ratio (drugs/weeks interaction) = 2.44; d.f. 10,210; $P = 0.009$.
2. F-ratio (weeks) = 0.79; d.f. 5,210; NS.
F-ratio (drugs/weeks interaction) = 1.96; d.f. 10,210; $P = 0.039$.

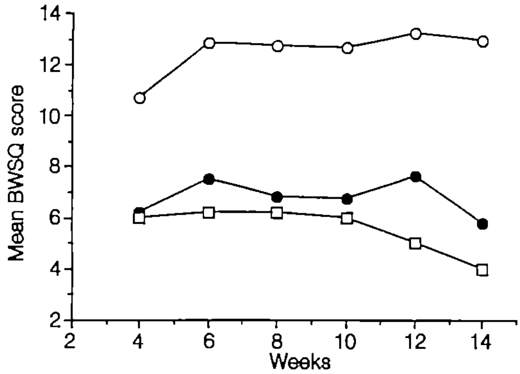

Fig. 3 Mean scores for withdrawal symptoms (BWSQ) in patients completing the full withdrawal programme who had received benzodiazepine treatment before entry to the study for >5 years (–○–; $n = 19$), 1–5 years (–●–; $n = 19$) and <1 year (–□–; $n = 7$).

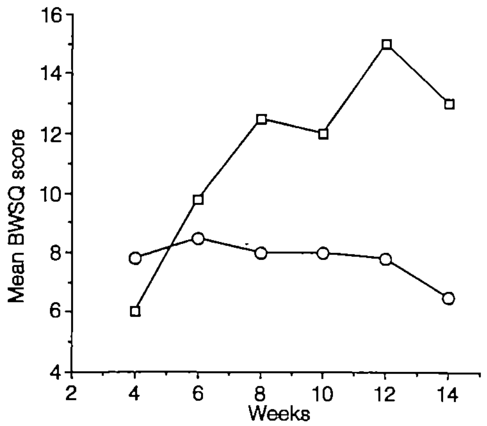

Fig. 4 Mean scores for withdrawal symptoms (BWSQ) in patients with personality disorder (–□–; $n = 8$) and those without personality disorder (–○–; $n = 33$) who completed the full withdrawal programme.

Table 3
Personality status of 59 patients (both those who completed and dropped out of the withdrawal programme) by diagnosis using Personality Assessment Schedule (PAS)

PAS personality disorder	Completers ($n = 41$)	Drop-outs ($n = 18$)
None	33	13
Passive–dependent	5	0
Anankastic	2	3
Schizoid	1	1
Sociopathic	0	1

$\chi^2 = 9.5$, d.f. 7, NS

there were 20 comparisons) they are of interest because despite the lorazepam group having these lower scores it had a greater drop-out rate.

For purposes of comparison both the dose of drug taken on entry to the study and the duration of treatment were used to divide the patients into three groups. Dosage was separated into mean daily dosage of less than 6 mg, 6–10 mg, and greater than 10 mg, and duration of treatment into 6–12 months, 1–5 years, and greater than 5 years. There were no significant differences between any of the scores for the three dosage groups following withdrawal, although those on higher dosage had generally higher scores. However, longer duration of treatment (>5 years) was associated with greater total mean scores on the CPRS ($F = 3.05$; d.f. 2,42; $P = 0.06$) and BWSQ ($F = 4.4$; d.f. 2,42; $P < 0.02$) (Fig. 3). Although BWSQ scores increased after withdrawal in the long-duration group they were also high before withdrawal at week 4.

Thirteen of the 68 patients were diagnosed as having a personality disorder using the PAS and nine others had insufficient information for full personality assessment. Five of these dropped out so that of the 41 patients who were fully assessed for personality status and who completed the study only eight were personality-disordered (Table 3). There was no significant difference between the proportions of drop-outs and completers who had personality disorders but of the eight completers five had passive–dependent personality disorders using the computer classification of the PAS. There was a highly significant personality–week interaction in BWSQ scores, with much higher scores after withdrawal in patients with personality disorders (Fig. 4) ($F=7.1$; d.f. 5,195; $P<0.001$). No such differences were found in CPRS and BAS scores with respect to personality status ($F=1.2$ and 0.9 respectively; d.f. 5,195; both NS).

Discussion

The results support the policy of gradual rather than rapid withdrawal of benzodiazepines in dependent patients (Tyrer *et al*, 1983; Ashton, 1984; Cantopher *et al*, 1990). The two-thirds success rate of complete withdrawal compares favourably with other studies in out-patients and primary care (Hopkins *et al*, 1982; Teare Skinner, 1982; Onyett & Turpin, 1988) but is not as high as the success rates of studies in which in-patient treatment is allowed (Petursson & Lader, 1981; Ashton, 1984). The relatively easy transition from the original benzodiazepine to the trial drug suggests that the dosage equivalents were at least not too low and that cross-dependence was strong. Although some patients had new symptoms on changeover the evidence that those who changed to the same benzodiazepine as the original compound had similar symptoms suggests that any difficulties in changing benzodiazepines were more likely to be due to psychological factors rather than physical dependence.

More patients dropped out when randomly assigned to lorazepam and although the difference was not significantly greater than for the other two benzodiazepines, when taken together with other evidence (Tyrer *et al*, 1981; Rickels *et al*, 1986), the findings suggest that even after only four weeks of treatment lorazepam is a more difficult drug from which to withdraw than bromazepam or diazepam. The suicide of one of the patients allocated to lorazepam may be regarded as a chance finding but a similar instance has been reported by Ashton (1987) and is a reason for concern.

The greater problems with lorazepam are unlikely to be simply explained by pharmacokinetics since bromazepam and lorazepam have almost identical elimination half-lives of 12–14 hours, but could be related to potency as lorazepam was the most potent of the benzodiazepines studied. The dosage equivalents chosen (lorazepam:bromazepam:diazepam 1:3:5) erred in favour of lorazepam being given in somewhat higher dosage than the other two compounds. A ratio of at least 1:10 is now considered more appropriate for equivalence of lorazepam and diazepam (Aranko, 1985).

Despite lorazepam being associated with a higher drop-out rate it did not have higher withdrawal symptom scores, and for two of the items in the BWSQ the scores for lorazepam were significantly lower than the other two benzodiazepines. Although this could be explained by those with the most marked withdrawal problems dropping out and not being represented in the figures, it also suggests that there may be some unusual properties of lorazepam that make it difficult for patients to tolerate withdrawal.

The recommendation that patients dependent on short-acting benzodiazepines should change to one of a longer half-life before withdrawal, of which diazepam is most commonly favoured (Tyrer *et al*, 1983; Ashton, 1984; Higgitt *et al*, 1985), does not receive much support from this study. The patients allocated to diazepam had no advantages over the other two benzodiazepines with regard to withdrawal symptoms (and their symptoms were somewhat more pronounced) (Fig. 2). This suggests that when gradual withdrawal over six weeks is possible by having graduated dose reduction there is no reason why other benzodiazepines (with the possible exception of lorazepam) should not be used. However, in practice diazepam is likely to remain popular for drug reduction because of its three dosage strengths.

The design of the study also allows some comparison to be made between other factors influencing the severity of withdrawal symptoms. Personality status was the most prominent predictor of withdrawal problems, and, as in other studies (Clift, 1972; Tyrer *et al*, 1983), there were more dependent personalities in those who had withdrawal symptoms. The findings support the claim that personality status is important in influencing the dependence potential of patients (Tyrer, 1989). On a more positive note, all the patients with dependent personality disorder completed the study despite their greater withdrawal symptoms, suggesting that such patients cope better with the distress caused by them. A similar finding has been shown in another recent study (Ashton *et al*, 1990).

Dosage of benzodiazepine on entry to the study was not a significant indicator of withdrawal problems and this is at variance with other data (Tyrer *et al*, 1988). However, the criteria for entry to the study ensured that all patients were taking a relatively low dose with an upper limit well below the equivalent of 30 mg of diazepam daily set at the upper limit for therapeutic dosage (British Medical Association and Royal Pharmaceutical Society, 1989). Total dosage taken (which correlates highly with duration) was a useful predictor of withdrawal difficulties although as patients who had taken their drugs for five years or longer had high withdrawal scores before reduction, some of these problems might not be true withdrawal symptoms. Ashton

(1984) has argued that patients can develop withdrawal symptoms while remaining on the same dose because of the development of tolerance, but an alternative explanation is that the level of anxiety is generally higher in long-term users and that this contaminates the measurement of withdrawal.

Taken together, the results show that personality status and total dosage of benzodiazepine consumed are the main influences on the intensity of benzodiazepine withdrawal symptoms, and that lorazepam is also more likely to cause difficulties in withdrawal than either bromazepam or diazepam.

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Management of First Episode Psychotic Illness in Afro-Caribbean Patients

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We studied retrospectively a consecutive series of 40 Afro-Caribbean patients and compared them with 40 non-Caribbean patients matched for age, sex, and diagnosis. There was no overall difference in initial or cumulative doses of neuroleptic medication in the early treatment of psychosis. However, a small subgroup of Afro-Caribbean patients received higher peak dosages. Clearly recorded episodes of behavioural disturbance were more frequent in Afro-Caribbean patients generally. They were more likely to be admitted compulsorily, discharged earlier, and prescribed depot medication.

There has been increasing recent awareness of psychiatric illness in ethnic groups in the United Kingdom (Littlewood & Lipsedge, 1982, 1988; London, 1986). Considerable debate has been generated about reported variations in phenomenology and classification of psychiatric conditions, and the extent to which these may reflect different aetiological factors, pathoplastic cultural effects, and racial discrimination.

A further area of concern has focused upon the management and treatment of psychiatric conditions in ethnic groups. Several studies, spanning nearly a decade, have consistently reported higher rates of compulsory admissions in certain ethnic groups in the United Kingdom, and have highlighted a tendency for greater police and lower primary care involvement in such admissions (Rwegellera, 1980; Harrison *et al*, 1984, 1989).

Attitudes of both doctors and patients to therapeutic measures such as interpretative psychotherapy are determined at least partly by the ethnicity of the patient. For example, it has been reported that in the United States, black patients are less likely to be considered for psychotherapy, suggesting that physicians employed stereotyped conceptions based upon ethnicity, both in their appraisal of patients and in their consideration of potential therapeutic measures (Thomas & Sillen, 1972; Cole & Pilisuk, 1976). In the United Kingdom, Littlewood & Cross (1980) found that psychotic Afro-Caribbean and Asian patients were more irregular in their clinic attendance and more likely to be seen by junior members of staff. With reference to medication, they reported that black patients more often received neuroleptic therapy compared with other psychotic patients matched for age, sex and diagnosis, and that a significantly higher proportion of black patients received depot maintenance therapy. In another study of 1752 out-patients from five different clinics in the United States, Adams *et al* (1984) reported that the mean dosage of neuroleptic received by Hispanic patients was similar to that received by white patients (431 mg of chlorpromazine daily, s.d. 611 mg), whereas black patients received a mean dosage of 535 mg of chlorpromazine daily (s.d. 830 mg). However, after correction for diagnosis the difference was found to be non-significant.

In general, studies comparing medication treatment between ethnic groups have been subjected to a number of limitations. For example, concurrent antidepressant and anticholinergic medications, both known to affect the bio-availability of neuroleptic medications (Grammer & Rolfe, 1972; Singh & Smith, 1973; El-Youself *et al*, 1974), are seldom controlled for. In addition, while it is generally assumed that neuroleptic requirements may change with time due to alterations in liver metabolism (Curry *et al*, 1970), few studies take into account the duration of previous treatment.

Besides issues of medication, the management of acutely disturbed psychotic patients involves decisions about admission to hospital, application of mental health act sections, control of behavioural disturbance, and judgements about the level of nursing supervision. Improvement in symptoms is followed by further decisions concerning discharge, maintenance therapy and follow-up arrangements. Most of these decisions involve complex judgements taking into account the social background, educational status, personality and family support of the patient, as well as the nature and course of the particular illness. It is also conceivable that the ethnic background of patients has an important influence in such assessments.

These issues, together with concern about excessive medication in patients from ethnic groups, have recently provoked considerable media attention.

Concern has been expressed that patients from certain ethnic groups receive differential treatment reflecting stereotyped responses by mental health service staff.

However, apart from anecdotal accounts, there are few reliable data relevant to issues of medication and the management of acute psychosis in patients from different ethnic backgrounds. Although medication issues may differ according to the diagnostic group, and in particular schizophrenia, public concern has been focused upon the treatment of psychosis in general. The present study was therefore carried out to investigate some of these issues in one ethnic group, Afro-Caribbean patients, presenting to the psychiatric service with a first episode psychotic illness. In particular, we wished to address whether there are differences between Afro-Caribbean and non-Caribbean psychotic patients in terms of:

(a) prescribed dosages of neuroleptic medication during the acute phase of the illness
(b) the proportion commenced on depot maintenance therapy after a first episode of psychosis
(c) the proportion admitted to hospital, the duration of admission and the use of compulsory procedures
(d) the degree of behavioural disturbance in the acute stage of illness.

Method

Our method of case finding has been fully outlined in a previous paper (Harrison *et al*, 1988). This was a two-year prospective study, including all patients of Afro-Carribean ethnic origin presenting for the first time with psychotic symptoms to psychiatric services from a defined catchment area in Nottingham. The study closely followed the methodology used in the recent World Health Organization study on early manifestations and first-contact incidence of schizophrenia in different cultures (Sartorius *et al*, 1986), for which Nottingham was a field centre (Cooper *et al*, 1987). Non-Caribbean patients from that study, identified using the same case finding methods and screening criteria, were used as a comparison group for the present consecutive series of Afro-Caribbean patients.

Details of the screening schedule for 'psychosis' were given in a previous publication (Harrison *et al*, 1988), although the major inclusion criteria were presence of (a) hallucinations, (b) delusions, (c) marked thought disorder, (d) marked psychomotor disorder, or (e) bizarre or grossly inappropriate behaviour; in the absence of an organic condition. The criteria were applied by the research team to symptoms recorded in case notes when possible candidates for inclusion in the study were identified. The 42 patients so included were given a Present State Examination (PSE; Wing *et al*, 1974) and accorded a 'certainty of schizophrenia' code on the basis of all the clinical information. Sufficient information was available regarding medication and early management for the inclusion of 40 of these patients in the present study. For the purpose of comparison, 40 patients were selected from the non-Caribbean series of psychotic patients, matched for age, sex and 'certainty of diagnosis' code for schizophrenia.

For each identified patient, medical notes, nursing records and prescription charts were obtained. Relevant data were systematically extracted from each document. These included: (a) demographic data (age and sex); (b) whether there was compulsory admission or detention under the Mental Health Act 1983 (including a section 5.2); (c) dates of admission and dates of discharge – patients not admitted to hospital within three months of contact are regarded as out-patients for the purpose of this study; (d) dosages and type of neuroleptic medication prescribed: (i) on admission, (ii) maximum dosage, (iii) on discharge, (iv) cumulative dosages over first four days, and (v) over first two weeks; and (e) whether and when depot therapy was instituted.

For the purpose of comparison, dosages of different neuroleptics were converted to equivalent dosages of chlorpromazine using the Davis table (Davis, 1974). The table does not contain data for zuclopenthixol and flupenthixol. In this study 400 mg of zuclopenthixol and 40 mg of flupenthixol were each regarded as equivalent to 25 mg of fluphenazine.

Evidence for behavioural disturbance and agitation was scored as number of clearly recorded incidents. These episodes were defined as follows: (a) actual violence to people (e.g. kicking a nurse); (b) actual violence to property (e.g. pulling a sink from the wall); (c) extreme bizarre behaviour (e.g. running naked in a ward); (d) serious threatening behaviour excluding verbal threats (e.g. pointing knives at people); (e) episode of successful absconding.

Data were analysed using the Statistical Package for Social Sciences (Nie *et al*, 1975). Data were not normally distributed and were therefore analysed using the Mann–Whitney U test and the χ^2 test, with one degree of freedom unless otherwise stated.

Table 1
Characteristics of Afro-Caribbean first-episode psychotic patients, compared with non-Caribbean control group

	Patients Afro-Caribbean ($n=40$)	Patients non-Caribbean ($n=40$)
Mean age (interquartile range): years	24.0 (21–30)	28.5 (21–40)
Sex		
male	24	26
female	16	14
Certainty of schizophrenic diagnosis		
certain	15	20
very likely	11	8
probable	3	4
possible	5	4
no schizophrenia	6	4

No significant difference at $P = 0.05$; Mann–Whitney U test, χ^2 test.

Results

The two groups matched for age, sex, and certainty of diagnosis are shown in Table 1.

Since control for diagnosis was based on a categorisation with reference to a schizophrenic diagnosis, it was necessary to inspect further the main diagnosis for the two groups with 'possible schizophrenia' and 'no schizophrenia', to ensure that they were comparable. The main ICD-9 (World Health Organization, 1978) diagnosis for patients within these levels of diagnostic certainty are listed in Table 2.

There was no significant difference between the proportion of Afro-Caribbean patients (75%) and the proportion of non-Caribbean patients (90%) receiving neuroleptic therapy at some point during admission, or within three months of making contact.

For those receiving neuroleptic treatment, there was no significant difference in the proportions who were on concurrent antidepressant and concurrent anticholinergic therapies (Table 3).

Table 2
Main diagnoses (ICD-9) for patients with 'possible schizophrenia' and 'no schizophrenia'

Main diagnosis (ICD-9)	No. of patients Afro-Caribbean ($n = 11$)	 non-Caribbean ($n = 8$)
Manic-depressive psychosis, mania	3	3
Manic-depressive psychosis, depression	2	3
Unspecified psychosis	2	0
Pathological drug-intoxication	2	0
Alcohol-dependence syndrome	0	1
Acute paranoid disorder	1	0
Adjustment reaction	0	1
Hysterical episode	1	0

Table 3
Pattern of pharmacotherapy in Afro-Caribbean and non-Caribbean patients receiving neuroleptic treatment

Medication	No. of patients on neuroleptics Afro-Caribbean ($n = 30$)	 non-Caribbean ($n = 36$)
Concurrent antidepressant therapy	3 (10%)	9 (25%)[1]
Concurrent anticholinergic therapy	20 (66.7%)	24 (66.7%)[1]
No. of neuroleptic drugs used in index episode		
one	10 (33.3%)	15 (41.7%)
two	16 (53.3%)	17 (47.2%)
three	4 (13.3%)	3 (8.3%)
four	0 (0%)	1 (2.7%)

1. No significant difference, χ^2 tests.

The number of different neuroleptic drugs employed for each patient during the index episode (either consecutively or concurrently) is shown in Table 3.

Frequency distributions of neuroleptic dosages (initial, maximum, discharge, and cumulative dosages over the first four days and the first two weeks) are shown in Fig. 1.

Further analysis of initial, maximum, and discharge dosages in patients with 'certain' and 'very likely' schizophrenic diagnoses ($n = 26$ in Afro-Caribbeans, $n = 28$ in non-Caribbeans) produced very similar patterns, with no significant difference between Afro-Caribbean and non-Caribbean groups (Mann-Whitney *U* tests).

Although comparisons on these measures produced no significant difference in dosages prescribed to Afro-Caribbean and non-Caribbean patients (Table 4), if the two groups are compared on the proportion of patients receiving maximum neuroleptic dosages above a given amount ('cut-off' dosage), a significant difference is obtained at 2000 mg chlorpromazine equivalent ($\chi^2 = 4.98$, $P < 0.03$) (Fig. 2). In other words, more Afro-Caribbean psychotic patients were treated with dosages above 2000 mg of chlorpromazine equivalent ($n = 9$), compared with the non-Caribbean group ($n = 3$).

To control the effect of the presence of behavioural disturbance (see below) in the two groups, a further analysis was carried out, focusing on patients with

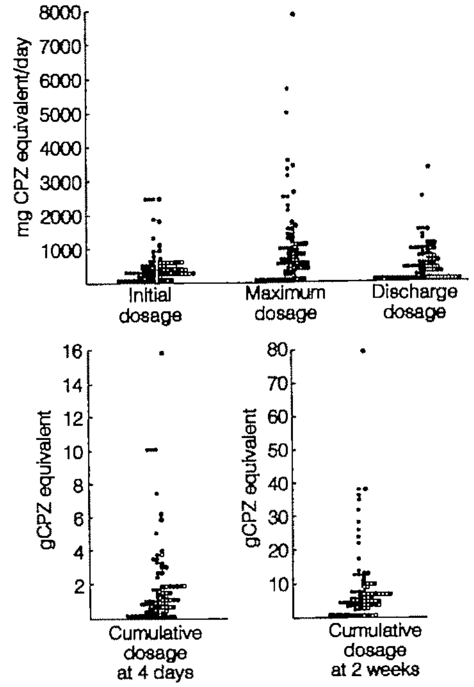

Fig. 1 Neuroleptic dosages (chlorpromazine (CPZ) equivalent for Afro-Caribbean (●) and non-Caribbean patients (○) with first-episode psychoses

Table 4
Relationship between neuroleptic dosage and ethnicity
(AC = Afro-Caribbeans; NC = non-Afro-Caribbeans)

Neuroleptic dosages: mg CPZ equivalent/day		Median	Interquartile range
Initial dosage	AC(n=30)	300	(200–535)
	NC(n=36)	357	(250–535)
Maximum dosage	AC(n=30)	915	(447–2142)
	NC(n=36)	810	(535–1250)
Discharge dosage	AC(n=25)	448	(298–892)
	NC(n=30)	535	(357–825)
Cumulative dosage (4 days)	AC(n=31)	1200	(600–2500)
	NC(n=36)	1600	(1000–2217)
Cumulative dosage (2 weeks)	AC(n=31)	5200	(2550–17129)
	NC(n=36)	6789	(4200–10300)

No significant differences at $P=0.05$; Mann–Whitney U-tests.

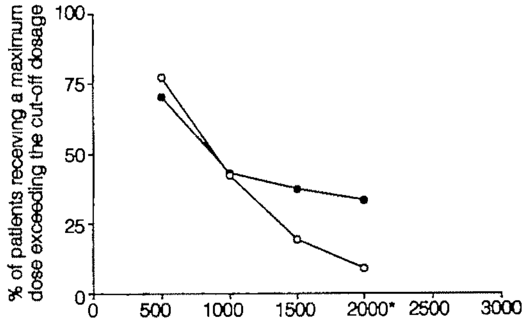

Fig. 2 Proportion of Afro-Caribbean (–●–) and Non-Caribbean (–○–) patients receiving neuroleptic therapy exceeding specified cut-off dosages (*$P<0.05$, χ^2 test).

episode(s) of behavioural disturbance. It was found that eight out of 24 (33%) 'disturbed' Afro-Caribbean patients received a maximum dosage of above 2000 mg chlorpromazine per day, whereas none of the 12 'disturbed' non-Caribbean patients were on a similar dosage ($P<0.03$, Fisher's exact probability test).

Twenty-four (60%) of the Afro-Caribbean group had one or more episodes of 'disturbance' as defined in our method, in contrast to 12 (30%) of the non-Caribbean group ($\chi^2=6.1$, $P<0.01$). Fifteen Afro-Caribbean (37%) had two or more episodes in contrast to five non-Caribbean (12%) patients ($\chi^2=5.4$, $P<0.02$).

Among psychotic patients receiving neuroleptic treatment, depot therapy was initiated after a first episode of illness in 16 (53%) of the Afro-Caribbeans and seven (19%) of non-Caribbeans ($\chi^2=6.9$, $P<0.01$). Depot therapy was initiated at different intervals after initial contact. The median duration of this interval was equal in both groups (20 days). However, it was noted that depot therapy was started on the day of initial contact in three Afro-Caribbean patients but in none of the non-Caribbeans.

Depot therapy is of particular relevance to patients with a 'certain' and 'very likely' diagnosis of schizophrenia. Further analysis of patients within these categories was carried out. Twelve out of 26 Afro-Caribbeans (46%) and five out of 28 non-Caribbeans (18%) were initiated on depot medication ($\chi^2=3.78$, $P=0.052$). The difference just fails to reach significance.

For patients with diagnosis of 'probable', 'possible' and 'not' schizophrenia, four out of 14 Afro-Caribbean (29%) and two out of 12 (17%) non-Caribbean were started on medication (no significant difference, Fisher's exact probability test).

Thirty (75%) of the Afro-Caribbean sample were admitted within three months of making initial contact, compared with 35 (87%) of the non-Caribbeans. The difference was not significant. For those admitted to hospital, the duration of stay had a median of 27 days (interquartile range 14–47) for Afro-Caribbeans and 50 days (interquartile range 32–60) for non-Carribeans ($P<0.02$, Mann–Whitney U test).

Twenty (50.0%) Afro-Caribbean patients were under a Mental Health Act section (including a section 5.2) at some point during their admission compared to nine (22%) non-Caribbean patients ($\chi^2=5.4$, $P<0.02$).

A total of 25% of Afro-Caribbean patients, compared with 10% of the non-Caribbean patients did not receive medication. This difference did not reach significance. A review of clinical notes suggested that although these patients met entry criteria for psychosis, most did not consent to treatment, and circumstances at the time did not warrant the use of compulsory procedures.

Discussion

The majority of Afro-Caribbean and non-Caribbean patients were started on antipsychotic medication at the first contact with psychiatric services.

The initial dose was usually prescribed at, or shortly after, first contact. It would be anticipated that at this stage any preconceived ideas based on ethnic stereotypes would be most likely to lead to bias. Our data showed no evidence of such bias. The results showed that for both Afro-Caribbean and non-Caribbean patients, the initial dose had a median of just above 300 mg chlorpromazine per day, at the lower end of the dose range considered effective in producing antipsychotic effects (Davis & Garver, 1978).

Looking at the maximum dosages, 90% of patients eventually received a dosage above 300 mg chlorpromazine per day. The maximum dosages are predominantly reflections of treatment of behavioural disturbance in the acute phase of illness. Our findings indicate that a subgroup of Afro-Caribbean patients ($n=9$) received a relatively high dosage of antipsychotic medication, although this subgroup did not significantly affect the overall central tendency of the dosage distribution indicated by the median.

The discharge dosage of neuroleptic is determined by a number of different factors, including the clinical state and the level of side-effects considered tolerable. Our results suggest that the perceived requirement for neuroleptics was also similar for the two groups at this point in their treatment.

Cumulative dosages (day 4 and 2 weeks) provided another perspective on the pattern of medication. Data on these confirm a lack of overall difference in the two groups.

Dosage analysis restricted to patients with 'certain' and 'very likely' schizophrenia produced similar results, although the numbers in each group (26 Afro-Caribbean, 28 non-Caribbeans) are relatively small.

We found a higher prevalence of behavioural disturbance in first episode psychotic Afro-Caribbean patients. A question raised by this observation is whether behavioural disturbance accounts for the use of high maximum neuroleptic dosage above the 2000 mg 'cut-off' in the subgroup of Afro-Caribbean patients identified. There is some evidence which suggests such a link. Most of this subgroup of Afro-Caribbean patients also showed behavioural disturbance (eight out of nine). However, we have already noted that 'disturbed' Afro-Caribbean patients are more likely to receive higher maximum dosages above the cut-off than 'disturbed' non-Caribbeans. This may indicate an ethnic bias in management or alternatively our method of categorising degree of 'disturbance' is not sensitive enough. Indeed, a review of the case-notes confirms that the Afro-Caribbean subgroup contains some of the most disturbed patients in the series. Unfortunately the numbers in our samples limited the use of multivariate techniques to further analyse the relative weighting of 'ethnicity' and 'disturbance' in 'high-dose' neuroleptic treatment.

Two previous studies have demonstrated that depot neuroleptic therapy was more prevalent among Afro-Caribbean patients (Littlewood & Cross, 1980; Glover & Malcolm, 1988). These studies reported on prevalence rates and therefore did not determine whether Afro-Caribbean patients were more likely to be prescribed depot therapy at onset or whether they remained on depot for longer periods. The present study demonstrates that depot therapy was initiated in a higher proportion of Afro-Caribbean patients after a first episode of illness.

Depot neuroleptic therapy has been shown to be effective in preventing relapse in schizophrenia (Hirsch *et al*, 1973). However, it is associated with long-term toxicity and the stigma of chronic patient status, and it is less flexible in dosage adjustment. Furthermore, a proportion of patients may never suffer a relapse even without maintenance therapy (Gardos & Cole, 1978). It is therefore of concern that over one half of Afro-Caribbean patients offered neuroleptic treatment were initiated on depot in their first episode of illness, compared with less than one-fifth of non-Caribbeans.

One important reason for prescribing depot therapy in preference to oral medication is consideration of compliance (Hirsch, 1982). It is not possible from the present data to determine whether prescription of depot medication was in response to observed non-compliance or to preconceived ethnic stereotypes. In our sample, three Afro-Caribbean patients were given test doses of depot injection in the first day of contact, suggesting that the latter alternative operated at least in some instances.

Our data confirm the findings of several previous studies (e.g. Ineichen *et al*, 1984; McGovern & Cope, 1987) that when admitted, Afro-Caribbean patients are more likely to be under compulsory procedures. The median duration of stay in hospital was significantly shorter for Afro-Caribbean patients, possibly reflecting a reluctance to stay in hospital. We acknowledge that factors influencing discharge are complex and this question could only be satisfactorily resolved with a prospective study.

Conclusion

Attempts to measure differences in the management of psychotic patients from different ethnic backgrounds pose several problems. A prospective study employing standardised assessment methods would yield more data, but the process of observation itself could distort the behaviour being measured. In the present study, data on management were recorded retrospectively and are therefore probably more valid measures of routine, spontaneous clinical practice.

Notwithstanding these possible limitations, the present finding suggest that there are few overall differences in oral neuroleptic therapy between Afro-Caribbean and control psychotic patients. Prescribing practice does not, therefore, appear to be directly affected by simple ethnic stereotypes.

There may be an exception in the small group of Afro-Caribbean patients who received maximum doses above 2000 mg chlorpromazine equivalent at certain stages in their management. Although this appears to have been related to behavioural disturbance, there remains the important question of whether stereotyped expectations of agitation played a part in subtle staff–patient interaction, which increased the likelihood of further 'disturbed' behaviour. These findings provide at least limited support for concern expressed about the medication of some Afro-Caribbean patients, and raise questions as to whether disturbed behaviour could be managed without resorting to higher doses of medication. In addition, the premature use of depot medication in some patients may decrease, rather than enhance, future compliance.

It is important, however, that these issues are not oversimplified. 'Disturbance' in psychotic patients represents a complex interaction of personal and social factors (see Harrison *et al*, 1989). Nevertheless, these findings, taken together with high rates of compulsory admission and use of depot neuroleptics, emphasise the need for a continuing audit of the psychiatric management of patients from different ethnic groups.

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Psychotic Depression: Psychoanalytic Psychopathology in Relation to Treatment and Management

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Jacobson's theory of affects and psychotic depression can be of benefit to the management of patients, even when recourse to physical therapies is required. Awareness of such psychodynamic issues would improve staff training, morale, and practice; rotation schemes for junior staff may have serious effects through the abandonment of patients and established therapeutic relationships.

This paper is an introduction to a way of thinking about psychotic depression which complements the more familiar biological, phenomenological, cognitive and psychosocial views (Pichot, 1988). It is an attempt to re-establish a connection in thinking between the somatic and psychological schools, in fact, to bridge the gap opened up by Jaspers (Conrad, 1952) by illustrating the value of single case study for utilitarian and heuristic reasons.

It would appear that there are two main reasons why, in the UK at least, such a bridging operation has rarely been attempted. The first is a history of antipathy towards the psychoanalytic view. This is partly due to an incomplete lay knowledge of the subject combined with a lack of opportunity to examine current psychoanalytic practice. This situation is beginning to improve as more analytically trained staff are appointed. Even when such dialogue is more possible, many will continue to have doubts about psychoanalysis – its method, rationale, and effects. Be that as it may, the analytical literature represents a repository of detailed single case studies unrivalled by any other branch of psychiatry and as such can be approached as a fund of psychopathology, whose value is independent of the efficacy of the therapy with which it is associated.

The second reason is that, just as biochemistry has had to develop its own esoteric language, so psychoanalysis has had to develop a language to describe the complex interactions both between people and between different aspects of the mind. This paper presents the variant of that language that best describes depression in all its manifestations (Stone, 1986).

The impetus for bringing together biological, cognitive and psychodynamic perspectives on chronic and severe depression was a larger study into such conditions (Scott *et al*, 1988). The author's role evolved into a threefold contribution:

(a) to give an overall psychodynamic perspective to the study
(b) to assess each case for suitability for psychodynamic therapy of a sort that can be realistically offered in a provincial centre – in this regard the criteria used were stricter than might be applied in more favoured centres
(c) to provide a psychodynamic commentary on each case.

Since the study began in 1980, profound and continuing changes in the pattern of provision of psychiatric care have taken place. These changes have been in the direction of a more multidisciplinary approach, less acceptance of medical perspectives and leadership and, because of the closing of the hiatus between in-patient care and out-patient contact through more available community resources, more continuing contact between staff members and patients. While there may be many benefits in these new arrangements, there are also problems (Bridges, 1990): in part the product of interdisciplinary rivalries, in part deriving from the absence of an effective *lingua franca* or common view of psychopathology which can accept the different perspectives of a social view, a psychological model or psychiatric diagnosis, yet meld these into a unified formulation of the patient which recognises not only the type and depth of the patient's psychiatric condition but also its likely evolution over time, whether treated or untreated.

Such an alternative perspective should also make a contribution to helping staff to understand the impact on themselves of working with depressed patients. This is of more importance given the more continuous nature of community care, since failure to attend to such issues contributes to poor morale in community mental health centres and staff 'burn-out'. Such a perspective should also illuminate the predictable problems of the effects on patients of the disruption to care by potentially lethal registrar rotation schemes (as illustrated in the case below).

Psychodynamic theory of affect and affective states

Of the psychoanalytical formulations of depression that have been developed, the theory that best serves the range of patients to be considered are those of Edith Jacobson. European-trained in the traditions of Kraepelin, Bleuler and Lange, throughout her extensive psychoanalytic clinical work with depressive patients before and after the introduction of electroconvulsive therapy (ECT), she never lost sight of clinical syndromes, and accordingly her psychoanalytical formulations are not vague generalisations regarding 'depression', but rather complex, specific formulations of the psychodynamics of the various syndromes.

This condensation of her work draws from her own updated papers (Jacobson, 1971) and Kernberg's (1980) review of her work. The essential elements of her formulations are outlined briefly, and these are then illustrated with reference to a patient who presented with severe psychotic depression.

Assuming a psychoanalytic structural view of mind in its aspects of conscious and unconscious mental functioning, Jacobson discussed depressive psychosis with reference to the superego, ego and id and mental energy in the classic analytical model, but developed this with reference to later concepts of ego psychology and object-relations theory. She elucidated the following points.

(a) It is helpful to differentiate between a theory of affects regarded as discharge processes (e.g. an outburst of rage) and a concept of affects as processes of tension reduction (e.g. the dysphoria of hunger setting in train a complex pattern of behaviour leading to eating and the reduction of hunger).

(b) Tensions can be unpleasurable or pleasurable, as can be the discharge of those tensions, and the "function of the pleasure–unpleasure principle is to produce an optimal oscillation between the polarities of tension and relief, thus contributing to the constancy principle by means of an everchanging, dynamically maintained optimal tension" (Kernberg, 1980). Both the rising and falling of tension is involved (e.g. precoital, coital and post-coital affect states).

(c) The mind functioning according to the reality principle is held to adjust the pleasure–unpleasure axis relative to external reality; pathological structures within the ego and superego, related to self and object representation, might severely distort this regulatory process. For example, in psychotic depression the pleasure role might be sacrificed, to adjust by means of a pathological 'optimal' tension to a distorted intrapsychic reality.

(d) Feelings are more than discharge states – they are complex and are richly coloured by drive investments in internalised self and object representation as well as by external reality.

(e) "Moods are diffuse, temporarily fixed affect states that involve the entire world of self and object representations and are both regulated and regulating. They are present both in normal and abnormal states and are profoundly influenced by libidinal or aggressive drive derivatives" (Kernberg, 1980).

(f) Normal moods are to be differentiated from pathological depressive moods by the predominance of aggressive drive derivatives in the latter. Moreover, the focused, cognitively delimited self-criticism of the mature superego in normal states is replaced by primitive, exaggerated superego control in pathological states.

(g) In psychotic depression there is a pathological refusion of self and object representations within both the ego and the superego which brings about the attack of a highly pathological, idealised, sadistic superego on a devalued and fused self-representation in the ego.

(h) The capacity for sadness, present in the mourning for a realistically or neurotically lost object, is absent in severe depression because of the pathological devaluation of the object and its psychological representation, which has been fused with a devalued self-representation. Only in the recovery phase can some depressives feel both depressed and sad as the capacity for feeling longing for a loved and unavailable object is regained.

(i) Jacobson reconfirmed the predominance of early oral and sadistic conflicts in depressed patients and the abnormally intense dependence on ambivalently loved, idealised and hated objects that are feared to be frustrating and rejecting.

(j) She proposed that the main anxieties and conflicts in depression are related to the fear of abandonment by the object and to related fears arising from the development of aggression towards the object when that object is both needed and frustrating. She delineated stages of defence against this narcissistic frustrating experience which relate to the clinical syndromes of depression.

While recognising the ever-changing dynamics involved, she went on to delineate four stages of depression of increasing severity associated with more profound disturbances of psychological structures and functions.

Stage 1 is characterised by increasing idealisation of the needed and frustrating object and a partial attempt to identify with it by self-idealisation in proximity to it. This involves denial both of the object's and the patient's aggression and frustration.

Stage 2. The collapse of the defence of stage 1 denial, in the face of continuing or increased distancing and therefore perceived abandonment, leads to stage 2, where the principal mechanism is that of a profound devaluing of the object and its representations. If this phase is partial and brief, increased autonomy from the object is achieved by angry self-affirmation. Under other circumstances the devaluation is destructive of the emotional investment in the object and the object representation in the self in such a way as to impoverish the self.

Whereas in neurotic depression, because tendencies to deny and idealise are less marked, self and object representations are more stable and reality testing is maintained, the pain of loss is sufficiently tolerated and compensated for to avoid further destruction; in psychotic depression this is not the case.

Stage 3. In psychotic depression the process goes into another stage in which there is again an attempt to idealise the object, although this time the attempts are more openly sadistic to wrench love from it, at the same time as ascribing strength and paradoxical badness to it. Side by side with this is masochistic self-devaluation. de Clerambault's syndrome can be understood as an eroticised variant of this stage.

Stage 4. The surfacing of such overt sadomasochistic aggression toward the ambivalently loved object precipitates the final psychotic stage. In this there is again devaluation of the object, although in this stage there is an introjection of the attributes of the object into both the superego and the ego. The superego is reinforced and becomes fused with the ideal, powerful sadistic elements of the object, while the weakened ego of the patient becomes fused with the, by now, devalued aspect of the object. The savage attacks of this primitive superego on the hapless ego over-rides reality testing in such a way that the merciless self-recrimination reaches delusional proportions since contact with reality is denied because the ego boundary with reality has been encroached on by the superego.

As is evident from the case illustration, traces of earlier stages remain evident in later stages of depression.

The extension of this theory into the depressions associated with schizophrenia and borderline states is beyond the scope of this paper.

Clinical case study

Mrs A, aged 40, was admitted for assessment from another unit where she had been admitted on six occasions over five years with severe depressive episodes and serious attempts at suicide. She had previously been treated with a variety of therapies, including ECT, a wide range of antidepressants and anxiolytics, and marital therapy. These had had but marginal, transient effect. She continued to present with persistent, pervasive, profound feelings of depression, hopelessness, guilt, worthlessness, uselessness and recurrent feelings that she would be better off dead than continuing to feel as she did. She dreaded waking each morning to such suffering, which also included intense apprehension, agitation and gastric churning. Her concentration was poor and she had no interests or energy. Her appetite and weight was variable. She continued to have frequent suicidal thoughts.

Her diagnosis was that of unipolar major depression with a complex combined mixture of features usually associated with a presumed biological cause but with seemingly reactive stressors in the form of her son suffering life-threatening chronic illness, and considerable marital conflict. In her brief interludes of comparative well-being, sufficient that is for her to be out of hospital, she had kept depressive feelings at bay by working at tasks until exhausted.

Past history and current circumstances

Mrs A was one of four siblings. Her parents were both full-time professional care-givers whom the patient portrayed as ideal parents. One of her sisters had committed suicide by means of a combined overdose of tricyclic antidepressants and monoamine oxidase inhibitors (MAOIs) after the failure of two marriages and periods of psychiatric care necessitating ECT. Mrs A vowed never to make such demands or to cause such distress to her parents.

She was married to a man who was supportive and attentive in her illness and whom she initially presented as being a marvellous husband. However, as emerged over the course of her admission, he was abnormally jealous, such that he had, for the greater part of their marriage, actively discouraged Mrs A developing social contacts or even maintaining links with her family on the grounds that the nuclear family should be entirely emotionally self-sufficient. The family, and Mrs A in particular, was therefore vulnerable to crisis through lack of social support. This occurred first in relation to the birth of their son and subsequently five years before this admission, when their son became very ill with a neurological condition, at first thought likely to become fatal. In fact he made a surprising, although partial, recovery. However, subsequently he developed an independent, chronic, life-threatening neoplastic condition. Mrs A coped well during the early crisis of her son's illnesses, but collapsed into her several suicidal depressions subsequently.

Progress of assessment interviews and management

Early in the first assessment interview Mrs A spoke of how she seemed to be unable to assert herself. Not merely was she unable, even when 'well', to assert herself, far less be aggressive, she was even aware that she 'absorbed' other people's aggression, particularly her husband's. She related how she felt that she had always conformed to other people's wishes, how that seemed the natural thing to do, given that her parents were so 'nice'. However, now she wanted to express herself, and that meant as far as she was concerned, to commit suicide.

During the second interview she said "I'm coming to realise that I have always been alone". She elaborated this by indicating that she felt that she had always 'given out' to others without being aware of her own needs, far less making sure that she received emotional support. Any resentment of this state of affairs was denied, as was any direct reference to her family of origin in this respect, although, apparently *apropos* of nothing, in the third interview she did remark how she envied other young girls on the unit because their parents came to visit them. In this third interview uncanny parallels were drawn between herself and her sister, how both had attempted suicide, and how this period of admission for a trial of combined tricyclic and MAOI antidepressants coincided exactly with the third anniversary of the death of her sister. Her sister was three years older than herself.

By the fourth interview it was clear that after an initial 'honeymoon' period following admission, Mrs A was again deeply depressed and in some measure more 'in touch' with her depression, freely voicing suicidal ideas, threatening both to walk out of the unit and to starve herself to death. She showed little sign of wanting therapeutic change or a therapeutic alliance, but if anything a perfect relationship with the therapist, while at the same time ensuring that her words and actions meant that she would be transferred from an open, psychotherapeutically orientated unit to a more secure organic/eclectic unit.

Here, in a more controlled environment, she became more settled on L-tryptophan, lithium carbonate, and phenelzine. By the time of her discharge, medication was modified to lithium carbonate (250 mg t.d.s.) and thioridazine (50 mg t.d.s.). Her psychological management, initially as an in-patient and latterly as an out-patient, was mainly in the context of conjoint marital sessions, where direct work was done to improve communication between the couple, to deal with problems as they arose, and to give both partners the opportunity to ventilate their feelings and grievances openly rather than such feelings finding expression in Mrs A's symptoms.

This approach enabled Mrs A to return home for a number of weeks but a change in arrangements necessitated by a change of registrars was associated with a further depressive relapse and an attempt at suicide. The decision was taken for Mrs A to be readmitted to her original hospital for continuing care and a last trial of cognitive therapy, which did not materially help.

In view of the total failure of combined medication and psychotherapies leucotomy was considered. Three months later a bilateral stereotactic subcaudate tractomy was performed at the Brook General Hospital, after which she felt an immediate improvement, with loss of her suicidal thoughts and dread of the following day. Over six months she recovered from lethargy and her marked post-operative morning agitation was controlled by trifluoperazine and diazepam. She needed no antidepressants. At follow-up 16 months later she remained well, off antidepressants but still needing diazepam to control the depressive symptom of gastric churning in the mornings.

Recent contact with her general practitioner revealed that during the subsequent nine years he has not had to see her for psychiatric problems; she has not only coped with her housework but returned to work. Her handicapped son is now in his early 20s and finding problems getting employment. To all outward appearances Mrs A's marriage is satisfactory.

Discussion

Psychopathology

At different times in their management of Mrs A, her clinicians varied in their own opinions as to whether she was severely ill by virtue of a biologically caused condition or severely depressed by marital difficulties compounded by her son's illness. Likewise, the same clinicians combined both the full range of biological treatments with a very full range of psychological and psychosocial treatments.

The psychopathology discussed in this paper makes no judgements as to whether the states and stages of depression described are of biological, psychological, or social origin. It does however begin to provide a framework into which these various elements can be seen to fit the pattern of a psychiatric syndrome. Moreover, although no claims are made for an overall causation of the clinical picture seen, attention is drawn to the active, usually unconscious, dynamics in the mind of the depressed patient which cause intrapsychic, attitudinal and enacted interpersonal effects. These in turn have an effect on the patient's own moods and feelings as well as those of family and attendant psychiatric staff.

The theory stresses the central role of affects rather than cognitions in the affective disorders. Not only are affects the faculty of mind most characteristically affected by these disorders, more fundamentally it is the pathological nature of these affects and the psychodynamic structures (both internal and external) controlling them which is of their essence.

A number of points stand out, in particular the complex interplay between loss, potential loss, dependency and aggression (f and j). Mrs A demonstrated most of the points listed above, particularly as experienced at the most psychotic end of the depressive range. Her affective tensions were mainly of a dysphoric nature of considerable intensity. She could achieve some oscillation in this state when its level became too high by discharging the affect in the process of an attempt at suicide (a–c). The different elements of dysphoria involved in the tension preceding and following such a discharge included aggression, guilt, and the feelings associated with a need for nurturance.

Her aggressive feelings were allowed, by herself and her family, no other outlet (j) than suicide. The pent-up frustrated anger therefore achieved high levels of tension which could only be controlled and contained further by the internal splinting effects of depression or by externally applied admission or medication with major tranquillisers. Alternatively, it could be released and discharged through her serious attempts at suicide. These recurrent attempts achieved tension relief for at most some months, before requiring repetition. A further effect of her attempts at suicide was to discharge her increasing feelings of guilt and worthlessness in an act of self-destruction to reduce the tension by an act of expiation.

Another related series of affects, besides aggression and guilt, whose tension levels were influenced by these acts were feelings associated with the giving and receiving of nurturance. Not only did her attempts at suicide mean she received more care and attention, but also they had the effect of removing her from the necessity for her single-handed care of her son for 'reasons' she could find acceptable, that is, to treat her own 'severe illness'.

In a parody of a nuclear family, all emotional or libidinal needs had to be met by other family members, other sources being systematically cut off by her husband's jealousy. The precarious give and take between husband and wife was first disturbed by the birth of their son, precipitating Mrs A's first depression. Slowly the pattern of family interaction rearranged itself, only to suffer the son's two illnesses. Either of these could have led to him dying and thereby withdrawing libidinal investment to the family as a whole and Mrs A in particular, who would then indeed be abandoned and bereft. At one level her subsequent feelings recall Dido's lament, "What is life to me if thou art gone?" Yet the son was not dead, and she had to cope with facing (unless, as she frequently was, she was in hospital) the person who 'threatens' to abandon her. Her suicidal acts were over-determined, but seemed to include elements of a pre-emptive strike to avoid the pain of loss, an attack on the son (stage 3), an identification with the dying object (stage 2) and (as in point c) the sacrifice of pleasure to achieve a pathological optimal tension.

Her capacity for identification with an abandoning object was eerily demonstrated at interview when she drew, with a note of triumph, the parallels of how, at the same age as her sister when she died, she was suicidal and being considered for combined anti-depressants. She amply demonstrated the complex oscillation of tension and relief (point b). Her suicidal ideas, freely expressed, as well as serving as an indicator of how she felt, discharged aggression on the staff and determined the degree to which she felt supported, controlled and punished.

Thus, despite, and arguably because of, the caring support given in an open unit, for few obvious external reasons she sent out signals that determined that she and her feelings should be firmly controlled in a more secure ward, where she soon settled but then complained of how punishing it was to be 'locked up'. When this point was reached, tension equilibrium was attained and requests were made for a transfer back to the open unit. This pattern seemed more than conscious manipulation – there was an institutional replication of her relationship with her husband. Leaving aside the psychopathology of her husband, he lived out in part the role of controlling, frustrating, punishing superego (c and f) but renounced this role for the more caring parental aspect of the superego when she was suffering; like the pathologically enlarged superego (stage 4), he had the effect of reducing her reality testing outside the family by actively cutting off affective and social bonds.

A striking component of Mrs A's account was her denial or lack of awareness of her own feelings and needs. She briefly exhibited a glimmering of insight regarding her own dependency needs, aspects of her husband's aggression, and her capacity for accepting aggression but not overtly expressing it. When she was apparently well, she maintained a stage 1 stance of denial of her own and her husband's aggression, combined with an idealisation of him and of their marriage. Moreover, she had no insight into the aggressive, controlling aspects of her suicidal threats and acts when ill and the degree to which other people's responses controlled her (e). Notably absent was a sense of sadness (h) regarding either her son's or her own predicament. Indeed, one was struck by a chilling objectivity.

Psychotherapy

This has been an account of one patient's psychopathology. No attempt was made at a psychodynamic psychotherapy beyond an attempt at marital sessions conducted more as conjoint management than in the expectation of dynamic change. Even at that level of involvement, it would seem that the disengagement of the junior staff involved with the couple represented an object loss which preciptated a further depressive episode (point j) and suicide attempt.

The salient factors weighing against the use of psychotherapy were her high suicide risk and an associated tendency to act out, her abysmal expectation of change, her low motivation for change, her fixed social setting containing a potentially imminent loss, her tenuous appreciation of the psychological components of her mental state, and her countervailing investment in external solutions to her problems. She amply demonstrated features of stages 3 and 4 of Jacobson's classification when stages 1 and 2 would mark the limit for psychotherapy even by experienced therapists under optimal conditions.

Not only the patient needs to be assessed for psychotherapy but also the putative therapist and the clinical setting. These include issues such as the personal and training experience held by the therapist as well as flexible psychiatric facilities sympathetic to and supportive of the vagaries of complex therapy. The chapters devoted to depression in Malan's (1979) *Individual Psychotherapy and the Science of Psychodynamics* are commended for further consideration of these issues. The temptation to ask a registrar or paramedic to "Go off and do a bit of psychotherapy with Mrs C because she is a nice lady with depression" should be resisted, particularly as the neediness of such patients can attract redoubled efforts. If staff are to take on cases, even at stages 1 and 2, they must be able to commit themselves for at least two years, to be closely supervised, and to enjoy good working relations with a clinical team.

Management

Whether or not psychotherapy is undertaken, an awareness of analytic psychopathology can inform management. It enables a proper, clear decision to be taken as to whether psychotherapy is a treatment option. If not, physical forms of treatment combined with informed humane management can be pursued more confidently and, if necessary, more vigorously. This is particularly important in the current climate of public opinion, when it is proving difficult to get consent for ECT or psychosurgery on the grounds that psychotherapy is preferable.

A psychodynamic insight gives an increased understanding of the family dynamics whereby it may become clearer as to whether the spouse is having a pathological effect in his/her own right, or whether he/she is being drawn in by the patient's pathology, or both. Moreover, such an awareness helps the recognition that patients have the capacity to replicate their inner mental life on the unit in the same way that they enact it at home. In this regard it has to be questioned and debated whether there are aspects of current patient management that could be improved. For example, could the incidence of patient abandonment be reduced? The effect of the rapid rotation of junior staff is to leave patients bereft of the doctor or staff member of first contact whom they have confided in and developed a relationship with at a critical phase of their illness. Conversely, could the effects of long-term contact with such patients be eased? It is not easy to cope with such patients' aggression, whether overt or covert, whether a punch in the face, legal proceedings for alleged negligence or, more often, insidiously draining emotional blackmail. The opportunity to talk through these experiences in supervision has often proved helpful in maintaining morale and broadening staff's knowledge base.

Study and research

Psychodynamic psychopathology conveys something of the progression of complex mental and interactional events across time. Sometimes that progression is rapid, an affective discharge can take only a few minutes, whereas affective shifts in others progressively unfold over years. Much research is based, understandably, on nomothetic 'snapshots' of populations. It is suggested that there is a wealth of opportunity to follow idiographically the course of changing mental states, as evidenced in both affect states and relationships (Weissman & Paykel, 1974) with reference to changes of medication and other interventions.

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Early Cortical Tactile-Evoked Potentials, Laterality and Schizophrenia

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No significant difference in the lateralisation of tactile-evoked potentials was found when a tactile stimulus was applied to the index finger of 14 schizophrenic patients and 14 age- and sex-matched controls. The early tactile responses, recorded from contralateral and ipsilateral parietal scalp electrodes, were compared. Our results differ from previously reported results.

Cooper *et al* (1985) reported 'abnormal' lateralisation of evoked potentials following tactile stimulation in 10 of 21 schizophrenic patients, relative to that in 15 normal persons and 8 patients with affective disorders. Comparing amplitudes, they found higher ratios of ipsilateral to contralateral responses following right and left tactile stimulation. We tried to replicate their study.

Short-latency somatosensory evoked potentials (SEPs) have a limited distribution in the region of somatic cortex contralateral to the side of stimulation (Williamson *et al*, 1970; Wiederholt, 1980; Desmedt & Brunko, 1980; Desmedt & Bourguet, 1985). Nevertheless, the literature is not consistent, since a number of papers reporting SEPs do discuss early ipsilateral components, but these are always of much smaller amplitude than the contralateral response and consistently slower (e.g. Salamy, 1978; Shagass *et al*, 1983; Tress *et al*, 1983).

Previous research into tactile-evoked potentials (TEPs) in psychiatry has also produced inconsistent results (Jones & Miller, 1981; Tress *et al* 1983; Shagass *et al*, 1983). The stimulus Cooper *et al* (1985) used was a loudspeaker, modified by cutting away most of the paper cone. The index finger rested lightly on the centre. We felt that the varying weight of each individual's finger on the loudspeaker could produce variations in the stimulus. Therefore we used a system where the tactile vibrator was supported on an arm pivoted in the centre which was counterbalanced by a weight at the other end. This produced a small upward force (of 1 newton) which was counterbalanced by the downward force of the finger. Extensive checks were made to ensure that the different stimulator did not alter the evoked potentials generated. Three subjects (normal volunteers) were tested in Nottingham and Sheffield. In addition, the loudspeaker used by Cooper *et al* was brought to Sheffield and retested with our equipment so that comparisons could be made. The shape, latency and amplitude of waves produced by the loudspeaker and our vibrator were essentially the same.

Method

Two cycles of a 200 Hz sine wave were fed to an amplifier which drove the vibrator head. The subject's forefinger rested lightly on the vibrator head but the finger was able to move freely. The weight of the arm and hand were taken by the arm rest. The static force applied by the vibrator head to the finger was constant at 1 newton. Stimuli lasting 10 ms were delivered every 0.8 s. The stimulus felt like a small tap.

Active electrodes were located at the vertex, central upper forehead, and one over the parietal cortex on either side, 7 cm lateral to the midline and 2 cm posterior to a line joining the vertex to the pre-auricular points. These active electrodes were all referenced to the ear lobes, where standard linked stick-on silver/silver-chloride electrodes were used. A metal-plate ground electrode was used on the ipsilateral forearm. All electrode impedances were less than 3 kohms. The bandwidth of the amplifiers was 0.5–100 Hz. Averaging was performed for 500 ms after the stimulus was presented. Usually 1000 responses were averaged per run. No habituation to the stimulus was observed.

Patients attended two sessions, usually one month apart. Each session began with a control run with the subject's finger near but not on the vibrator head and with popular music played through earphones masking the noise of the movement of the vibrator head. The apparatus was covered. The subject lay on a bed with eyes closed and all lights off.

Each subject had four further tests, first testing one hand, then the other, and then reversing this order. The order of testing hands was counterbalanced between subjects and patients. Every subject was tested at the same time of day and the temperature of the room remained constant. Arm lengths were measured.

Subjects

Results were obtained for 14 schizophrenic patients. All patients had been selected from the out-patient clinic, an acute admissions ward and a hospital where the more chronically ill were placed. All met DSM-III criteria for schizophrenia (American Psychiatric Association, 1980). Normal subjects were volunteers. Patients and volunteers were matched for age and sex. Mean age of patients was 39.4 years (range 28–52), and of controls was 38.9 years (range 30–57). Eleven were men and three were women. The age of onset of schizophrenia in the patients ranged from 4 years to 33 years. Ten patients had first developed the illness more than ten years ago, two between six and ten years ago, and two between two and five years ago. One patient only was unmedicated. Of the other 13, four were taking anticholinergics and one antidepressants; all took neuroleptics. Patients were subtyped as follows: disorganised type, three; catatonic, one; paranoid, five; undifferentiated, three; residual, two.

Results

The waves in the first 70 ms after the stimulus was presented were compared. The expected two positive peaks, P1 and P2, were seen in most subjects. P1 was recorded on the contralateral parietal cortex between 26 and 39 ms, P2 between 40 and 59 ms. The convention of Donchin *et al* (1977) in labelling the waves according to their latencies and their positive or negative sign was not followed, as reporting results became too complicated owing to different latencies for different subject groups. The amplitude (in μV) of the P1 and P2 waves were measured by taking the previous negative wave and measuring from that negative trough to the next positive peak. Figure 1 shows a typical early contralateral response for a TEP.

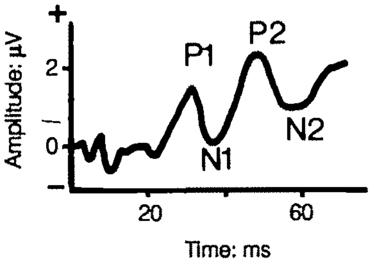

Fig. 1 Typical contralateral response to tactile stimulation of index finger showing P1 and P2 waves separated by N1. Stimulus artefact can be seen at beginning of trace.

The P1 and P2 mean latency values recorded on the primary receiving cortex were 32.4 and 50.9 ms for controls (on stimulation of the right hand). Patient mean values were similar, at 34.2 and 53.2 ms respectively. Not all subjects had both these waves. Table 1 shows figures of the number of people in whom responses were observed for each category of wave. Only the contralateral P2 wave evoked from stimulation of the right hand was observed in all subjects. The P1 contralateral wave to stimulation of the right hand was seen in 13 controls and 11 patients. Since the distribution of amplitude values was slightly skewed, median, range, maximum and minimum values are quoted in Table 1. The median amplitude value for controls (right hand stimulation) for the contralateral P1 wave was 1.6 μV (range 0.3–4.2). Patient values were similar. Differences between the mean value for patients and controls of all parameters of waves presented in Table 1 (where numbers were sufficient for the test to be valid) were not significant. Comparison of parameter values for left- and right-sided stimulation for each individual showed that the amplitude and latency of the P1 and P2 contralateral responses on the left and right parietal cortex were very similar. Mean latency for the P2 wave evoked from the left parietal cortex in the control group was 49.7 ms, and from the right parietal cortex 50.9 ms. The patient mean left/right latency comparison was within 1 ms.

Ipsilateral waves were not seen consistently in all subjects. An ipsilateral potential was judged to be absent if there was no potential seen within a window of -5 to $+10$ ms of the contralateral latency. A latency delay was observed between contralateral and ipsilateral measurements of 3–7 ms. The P2 contralateral/ipsilateral latency difference was 4.6 ms (stimulation of the right hand) for controls. This difference was significant, ($P < 0.02$), but a similar difference (of 4.9 ms) was found in patients ($P < 0.02$).

There was no significant difference in the mean arm length of controls and patients.

The Contralateral/Ipsilateral comparison

Where the contralateral response was present but the ipsilateral response was absent, it was easy to say that lateralisation was 'normal'. Individual variation was great, so a clear definition of 'abnormal' evoked response was required to apply the same criteria to both control and patient groups. Below several different definitions of 'abnormal' lateralisation are put forward, but in each case the same definition is applied to patient and control groups, enabling an objective comparison. These definitions are based on the ratio of contralateral to ipsilateral amplitudes. These ratios have been calculated only as an aid to defining an 'abnormal' response. The actual comparisons between control and patient groups have been done using Fischer's exact test on the numbers of subjects in each group having normal or abnormal evoked responses.

If 'abnormal' laterality is defined as the ipsilateral response being of a similar size to the contralateral, it can be expressed numerically and a contralateral : ipsilateral ratio less than or equal to one is judged 'abnormal'. Unilaterally abnormal means that this ratio has been found on one side only, whereas bilaterally abnormal means that this ratio has been found on both left and right parietal cortex. Using this definition, no controls or patients demonstrated the bilateral abnormality, and only one control showed the unilateral abnormality. These contralateral : ipsilateral ratios vary. It was quite common for a person to have a contralateral : ipsilateral ratio of less than one for one run and above one for another. A Fisher's exact test on the type of evoked response (normal or abnormal) showed no significant difference between our 14 patients and controls ($P = 1.0$). This is the definition Cooper *et al* appear to have used when defining 'bilateral abnormality'. In contrast to our results, ten of their schizophrenic patients (half) and none of their controls showed the bilateral abnormality.

Table 1
Contralateral and ipsilateral P1 and P2 tactile-evoked potential values of amplitude and latency for control and schizophrenic patient groups

	Controls ($n=14$)				Patients ($n=14$)			
	contralateral		ipsilateral		contralateral		ipsilateral	
	P1	P2	P1	P2	P1	P2	P1	P2
Right hand stimulated								
Latency: ms								
mean	32.4	50.9	35.7	56.0	34.2	53.2	32.5	58.0
s.d.	2.2	3.9	3.7	5.3	2.9	4.2	5.5	5.3
Amplitude: μV								
median	1.6	1.6	0.5	1.0	1.4	2.4	0.9	0.8
range	3.9	3.7	1.2	2.4	1.6	3.7	0.7	1.8
maximum	4.2	4.3	1.4	2.7	2.2	4.1	1.2	2.2
minimum	0.3	0.6	0.2	0.3	0.6	0.4	0.5	0.4
No. of subjects[1]	13	14	7	10	11	14	2	7
Left hand stimulated								
Latency: ms								
mean	31.8	49.7	35.0	56.0	32.2	52.6	38.0	59.0
s.d.	2.8	4.5	3.7	7.9	2.9	5.8	6.0	8.1
Amplitude: μV								
median	1.1	1.4	0.4	1.0	1.2	2.3	0.6	1.0
range	5.0	2.7	0.4	1.9	1.4	3.9	0.3	1.0
maximum	5.5	3.2	0.6	2.2	2.3	4.4	0.7	1.2
minimum	0.5	0.5	0.2	0.3	0.9	0.5	0.4	0.3
No. of subjects[1]	12	14	3	9	9	12	2	6

[1] In whom responses were observed for each category of wave.

Redefining 'abnormal' laterality so that an ipsilateral amplitude of 70% of the contralateral is 'abnormal', we found one control demonstrating the bilateral abnormality, and three controls showing the unilateral abnormality. Only one patient had the unilateral abnormality and none the bilateral abnormality (Fisher's exact test, $P=0.3$).

If 'abnormal' laterality is defined as a significant ipsilateral wave that can be clearly seen, of magnitude more than 50% of the contralateral amplitude, Fisher's exact test similarly applied still gave non-significant results ($P=0.17$). This is the definition that Cooper *et al* (1985) used for unilateral abnormality. Defined thus, one of our controls had the bilateral abnormality and four others had the unilateral abnormality. None of our patients demonstrated the bilateral abnormality and only one had the unilateral abnormality.

No matter in which of the above ways the contralateral: ipsilateral ratio is defined there was no significant difference between the number of patients and controls having different types of lateralisation (unilateral and bilateral abnormality grouped together versus normal). Cooper *et al* reported a χ^2 result as $P<0.01$ (their analysis included affective illness also). Clearly their results are very different from ours.

Variation within and between sessions

Visual assessment of wave data showed that intersession and intrasession stability was good for latency, but testing experience cast doubt on amplitude as a reliable unchanging measure, as can be seen in one striking example in Fig. 2. The two traces shown were made within 15 minutes of each other. Graph A had a P2 of 2.2μV, graph B a P2 of 5.2μV. The amplitude had more than doubled in 15 minutes for no apparent reason and no change in testing conditions. Latency remains stable at 50 ms.

Each session consisted of at least two runs specific to each individual's hand. Data were compared for stability of amplitude and latency over one hour. The change in amplitude was analysed by using the ratio of the first minus the second measurement of amplitude over the first. Table 2 shows the mean change in ratio expressed as a percentage. The results show much greater variation in the amplitude than latency measurements. There was no significant difference between the patient and control groups. No habituation to the stimulus was seen. Measurements of

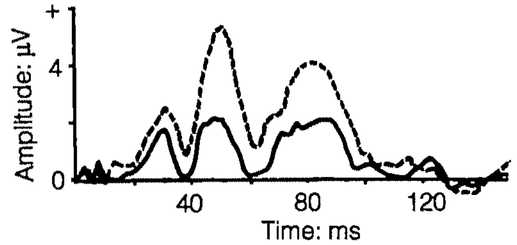

Fig. 2 Contralateral tactile-evoked potentials of one control subject. Note P2 wave amplitude variation between graph A (- and B (—); the time interval between A and B is 15 minutes. The latency remains stable at 50 ms.

Table 2
Mean percentage change in amplitude and latency of tactile-evoked potentials within a session

	Amplitude		Latency	
	P1	P2	P1	P2
All controls ($n=26$)	27	41	3	4
Schizophrenic patients ($n=14$)	37	44	5	6

There was no overall tendency for change in amplitude or latency to be in any one direction. No habituation to the stimulus was shown. All data are for the right hand being stimulated, with the contralateral response evoked from the left parietal cortex.

amplitude and latency were as likely to increase as decrease. Each patient was tested twice at an interval of approximately one month and these data showed a mean intersession variation of 30% in amplitude and 4% in latency over that time.

Discussion

The studies by Cooper *et al* (1985) were repeated but with different results. We did not obtain any significantly different latency or amplitude measurements or patterns of laterality in schizophrenic patients compared with controls. Cooper *et al* (1985) stated that most schizophrenics with a poor social outcome showed a marked lack of expected patterns of laterality. Our patients rated similarly on overall course of symptoms, their social functioning and work before testing (see Cooper *et al*, 1985, for details). Nine out of 14 of our patients fell into the 'worst outcome group'. Such a proportion does not differ significantly from that in Cooper *et al*'s sample. Our patient sample had a greater mean number of years since onset of the disease, so it would be expected that our more chronically ill sample would have at least demonstrated a similar lack of laterality.

Neither Cooper *et al*'s nor our experiment controlled for possible effects of medication. The number of unmedicated patients in our sample is too small to allow comment, but Cooper *et al* suggested that the type of response was not related to medication. There do not appear to be major differences in medication between studies.

While the results are negative, this paper does contribute to the whole discussion of ipsilateral/contralateral responses. Desmedt *et al* (1987) point out that scalp evoked potentials are now viewed "as composite profiles made up of distinct components that reflect activation of different neurons in the afferent pathway (far-field components) or cortex (near-field components)". It is difficult to assess the relative contributions of these components using single SEP traces. Fig. 3 shows that the distribution of the contralateral evoked response is more widespread than just the somatosensory receiving area: it is also observed at the vertex and ipsilateral electrode sites. However, the delay in latency from contralateral to vertex to ipsilateral sites is too great to be explained by volume conduction. The complex source and nature of the TEP does imply that its amplitude and latency can vary with different electrode positions.

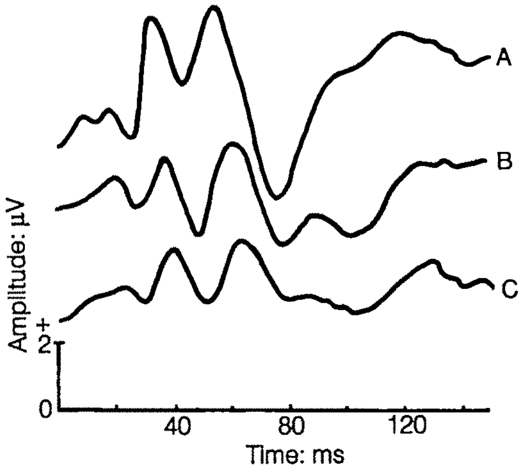

Fig. 3 Tactile-evoked responses to stimulation of right index finger in one normal subject at three different electrode positions: (A) contralateral parietal, (B) vertex, (C) ipsilateral parietal. Note the delay in latencies of P1 and P2 and diminishing amplitudes from contralateral to vertex to ipsilateral electrode positions.

Both Desmedt & Bourguet (1985) and Duff (1980) have warned against giving undue significance to single SEP waveforms. Ipsilateral potentials likewise have to be related to potentials in surrounding areas before they can be confidently interpreted.

To conclude, no patterns of ipsilateral/contralateral responses that could be specifically related to a schizophrenic population were found, although a number of the difficulties involved in interpreting early ipsilateral potentials did become apparent.

Acknowledgements

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Auditory Selective Attention and Event-Related Potentials in Schizophrenia

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Brain ERPs were recorded in ten unmedicated schizophrenic patients and age- and sex-matched healthy controls during a multidimensional listening task. Patients showed a marked reduction in a long-duration attention-related negative ERP component, termed 'processing negativity' (PN), which was elicited by attended stimuli. The amplitude of PN was significantly correlated with SANS and SAPS scores of schizophrenic symptoms. The P300 component was also reduced in amplitude in patients, and was significantly correlated with SANS ratings of negative thought disorder. These findings provide neurophysiological evidence of impairment in the maintenance of selective attention and the cognitive processes associated with target detection among schizophrenic patients. The reduced PN in schizophrenics implicates frontostriatal pathways in the aetiology of attentional deficits in schizophrenia.

Attentional deficits have been seen as a fundamental feature of schizophrenic psychopathology since Bleuler first described the 'group of schizophrenias' 80 years ago (Bleuler, 1911). However, the impaired performance frequently observed when schizophrenics perform attentional tasks could also reflect deficits in motivation or organisation of motor activity (Nuechterlein & Dawson, 1984). Neurophysiological indices of attention can be derived from scalp recordings of event-related potentials (ERPs), using paradigms which allow the effects of selectively attending to relevant stimuli to be distinguished from concurrent changes in general alertness or the effects of making an overt response (Hillyard *et al*, 1973). Further studies in healthy subjects have identified an early-onset negative component, termed processing negativity (PN), which is elicited by auditory stimuli to which attention is directed (Naatanen & Michie, 1979; Hansen & Hillyard, 1980). A later, parietal-maximal positive component, termed P300, is elicited by infrequent, task-relevant stimuli, which require a cognitive and/or motor response (Pritchard, 1981).

Hansen & Hillyard (1983) demonstrated that the PN component is extremely sensitive to the ease with which normal subjects discriminate auditory stimuli that differ on simple physical cues. Subjects listened to tone pips presented through earphones to either ear. Half the tones in each ear were of low pitch, the other half of higher pitch. Subjects were required to attend to a particular pitch/ear combination and press a button whenever they detected an occasional longer-duration (100 ms) 'target' tone among more frequently occurring 'standard' (50 ms) tones. By analysing ERPS elicited by standards, which never required an overt behavioural response, electrophysiological measures were derived which were uncontaminated by neural processes underlying response preparation. Standards which matched the target on an easily discriminated cue (e.g. tones delivered to same ear as the target) elicited an early-onset PN compared with tones delivered to the unattended ear. Standards which also matched the target on the more difficult to distinguish cue (e.g. tones of the same pitch and delivered to the same ear as the target) elicited an additional later-onset, long-duration PN. Standards delivered to the unattended ear elicited similar ERPs, regardless of pitch. Results obtained using this task are consistent with the operation of rapid, early selection, based on easily discriminated stimulus characteristics (Hillyard & Hansen, 1986).

Few studies have utilised selective attention paradigms in investigations of schizophrenia, and none have evaluated the late PN component. Previous studies have reported that significant early PN, around 100–200 ms after the stimulus, is elicited by attended stimuli in medicated (Baribeau-Braun *et al*, 1983; Hiramatsu *et al*, 1983), but not unmedicated (Kameyama *et al*, 1987) schizophrenics.

There is an extensive literature attesting to reduced P300 amplitudes in schizophrenics, obtained in a variety of experimental paradigms using auditory, visual and somatosensory stimuli (Pritchard, 1986). Some investigators have reported associations between P300 amplitude and clinical improvement following neuroleptic medication (e.g. Duncan *et al*, 1987), while P300 amplitude reduction has also been associated with other psychiatric diagnoses, such as depression and dementia. Further studies in unmedicated patients are required to establish whether reduced P300 amplitude reflects a generalised cognitive deficit or specific schizophrenic symptoms.

In the present study, a multidimensional listening task was used to examine hypotheses concerning attentional deficits in schizophrenia. For example, Venables (1964) suggested that schizophrenics are unable to ignore irrelevant stimuli. Support for this hypothesis would be provided if schizophrenics' ERPs showed a PN differential on the unattended ear between stimuli which were of the same pitch as the target and those which were not.

To assess the utility of ERP measures in investigating attentional deficits in schizophrenia, we wished to examine the relationship between ERP measures and ratings of psychopathology. Despite the small sample size of the present study, correlations were investigated between measures of PN and P300 amplitude and ratings of thought disorder and total ratings of schizophrenic symptoms.

Method

Three in-patients and seven out-patients who met DSM–III (American Psychiatric Association, 1980) and ICD–9 (World Health Organization, 1978) criteria for chronic schizophrenia were tested (9 men, one woman, mean age 31.0 years, range 22–58). All of the patients had received no antipsychotic medication during the previous six months and three had never received neuroleptics. Previously medicated patients were medication-free because of non-compliance or because their symptoms were not alleviated by neuroleptics. Mean duration of illness was 9.4 years (range 2–20). Eight of the patients were classified as 'chronic residual' under DSM–III, and the two remaining patients were diagnosed as 'chronic paranoid' and 'chronic with acute exacerbation, disorganised type'. At the time of testing, mean total symptom score, assessed using the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962), was 37.8 (range 26–53), reflecting moderate symptoms. A urine drug screen was performed to exclude patients whose symptoms may have been related to acute drug abuse.

Ten age- and sex-matched healthy controls were selected from hospital staff and volunteers who were well known to the research team. None had a history of psychiatric illness or drug abuse. Audiometric screening was carried out in both groups of subjects to exclude those with significant hearing loss.

Patients were interviewed by an experienced research psychiatrist (SVC), who rated patients on the Scales for Assessment of Positive and Negative Symptoms of schizophrenia (SAPS and SANS, respectively; Andreasen, 1982, 1984) based on information obtained during a structured interview and from case notes. These scales include global ratings for positive 'formal' thought disorder and negative thought disorder or alogia, as well as summary scores comprising ratings of hallucinations, delusions, bizarre behaviour and positive formal thought disorder (for the SAPS) and affective flattening, alogia, avolition, anhedonia and attentional impairment (for the SANS). The rater was blind to ERP findings while carrying out the clinical assessment.

The auditory attention task employed in this study was adapted from Hansen & Hillyard (1983). Subjects listened to tone pips (75 dB sound pressure level) presented through earphones to either ear. Half of the tones in each ear were low pitch (1047 Hz) and half were high pitch (1319 Hz). For each pitch/ear combination, 28% of the tones were of longer duration (100 ms) than the remaining 'standard' tones (50 ms). Tones were delivered in random sequences at intervals of 200–500 ms, so that stimuli at each pitch/location combination occurred with equal probability. Subjects were instructed to attend to a particular pitch/location combination (e.g. high pitch/right ear) and press a button whenever they detected an occasional longer-duration 'target' tone among the 'standard' tones. Tones at each of the four pitch/location combinations were attended during different runs. Subjects completed two runs of each attention condition, one responding with the left hand and one responding with the right hand. Each run lasted approximately 1.5 mins and included approximately 30 targets.

An electroencephalogram (EEG) was recorded from electrodes at pre-frontal (Fpz), frontal (Fz), central (Cz) and parietal (Pz) locations along the midline, along with vertical and horizontal eye movements for artefact detection, all referred to a standard potential from linked ears, and amplified using a Grass Model 12 Neurodata system with a bandpass of 0.01–30 Hz (−6dB attenuation points of −6dB/octave passive filters). Overlapping EEG epochs (duration 1280 ms, including a 250 ms pre-stimulus baseline) were averaged after rejecting those contaminated by artefact (vertical or horizontal eye movements exceeding 64 μV) or incorrect behavioural responses, either targets not followed by a button-press response (misses) or button presses following non-target stimuli (false alarms). ERPs were averaged by classifying stimuli according to whether they matched or did not match the nominated target stimulus on a particular run in terms of location (referred to as L+ and L− respectively), pitch (P+, P−) and duration (D+, D−). Thus L+P+D− refers to short-duration stimuli having the same location and pitch attributes as the target (L+P+D+).

Statistical analyses were carried out using repeated-measures analysis of variance (BMDP2V), and the probabilities reported were obtained following Greenhouse–Geisser adjustment (ϵ) of degrees of freedom to allow for violation of sphericity (Vasey & Thayer, 1987). Significant interactions were examined by calculating multiple comparisons using separate error estimates for each contrast. The Bonferroni argument was used to determine significance, with family-wise α set to 0.05.

Results

Scores for positive and negative symptoms are reported in Table 1.

Schizophrenics performed the task less accurately than controls (64% v. 78% hits; $P<0.05$; 4.9% v. 1.2% false alarms; $P<0.002$) and tended to respond more slowly (means (s.d.): 618 (76) ms v. 558 (82) ms, $P=0.09$). Patterns of false alarms were examined for both groups. In controls, 27.9% of false alarms occurred 200–1500 ms following L+P+D− stimuli, versus an average of 16.3% for the other equiprobable standards. The pattern for schizophrenics was similar: 27.7% following L+P+D−

Table 1
Global scores and total scores for ratings of positive (SAPS) and negative (SANS) symptoms

	Mean	Range
SAPS		
Hallucinations	1.0	0–3
Delusions	2.3	0–5
Bizarre behaviour	1.1	0–5
Positive 'formal' thought disorder	2.5	1–4
Total	6.9	2–14
SANS		
Affective flattening	2.4	1–3
Alogia	3.2	3–5
Avolition	3.5	3–5
Anhedonia	3.5	2–5
Attentional impairment	2.1	0–5
Total	14.7	8–22

versus an average of 16.2% following the other three classes of standard stimuli. These results suggest both schizophrenics and controls found the duration dimension most difficult to discriminate and indicate that patients were attempting to follow task instructions.

ERPS to standard tones

Group mean ERPs of controls to standard tones (Fig. 1(a)) showed an early PN (onset 60–70 ms after stimulus), elicited by L+P+ and L+P− standard stimuli, which was prominent at Fpz, Fz, and Cz electrodes. Schizophrenics showed a similar, although smaller, early PN. When measured as the mean amplitude over 100–200 ms after the stimulus, early PN was significantly larger for stimuli at the attended location (L+) than stimuli at the unattended location (L−) (stimulus main effect: $F(3,54)=19.01$, $P<0.0001$, $\epsilon=0.73$). The group × stimulus interaction was not significant ($F(3,54)=1.57$, $P=0.21$, $\epsilon=0.73$). However, a significant group × stimulus × electrode interaction was found ($F(6,108)=3.66$, $P<0.02$, $\epsilon=0.51$). Multiple comparisons at each electrode were calculated for L+ ERPs (100–200 ms epoch), and revealed significantly smaller mean (s.d.) early PN in schizophrenics ($-0.50(0.69)\mu$V) than controls ($-1.37(0.61)\mu$V) at the vertex (Cz) electrode ($P<0.05$ with Bonferroni correction).

The most striking differences between the group mean ERPs was the marked reduction of late PN in schizophrenics. The late PN was elicited by L+P+D− stimuli (i.e. the stimuli which were subjectively the most difficult to discriminate from the attended targets) in controls and was prominent at anterior scalp locations. A preliminary series of repeated-measures ANOVAs was calculated for 100 ms epochs from 200–1000 ms. No significant group main effects or interactions were observed in the 200–300 ms or 300–400 ms epochs. However, group effects were present for each subsequent 100 ms epoch, up to 1000 ms after the stimulus.

As a means of summarising the group differences in this latency range, late PN was defined and measured as the mean amplitude over the 400–1000 ms epoch. Late PN was significantly larger for L+P+D− stimuli than other standard stimuli (stimulus main effect: $F(3,54)=12.25$, $P<0.002$, $\epsilon=0.65$). The group × stimulus interaction was significant ($F(3,54)=3.72$, $P<0.04$, $\epsilon=0.88$), as was the group × electrode × stimulus interaction ($F(6,108)=3.07$, $P<0.03$, $\epsilon=0.63$): multiple comparisons were performed on mean amplitudes for L+P+ ERPs at Fpz, Fz, and Cz electrodes, and significantly reduced mean (s.d.) amplitudes in patients (0.05(0.61) v. $-1.09(0.99)\mu$V) were only found at the Fz electrode ($P<0.05$ after Bonferroni correction). There were no significant differences in late PN between L−P+ and L−P− ERPs for either controls or schizophrenics at Fpz, Fz, or Cz electrodes.

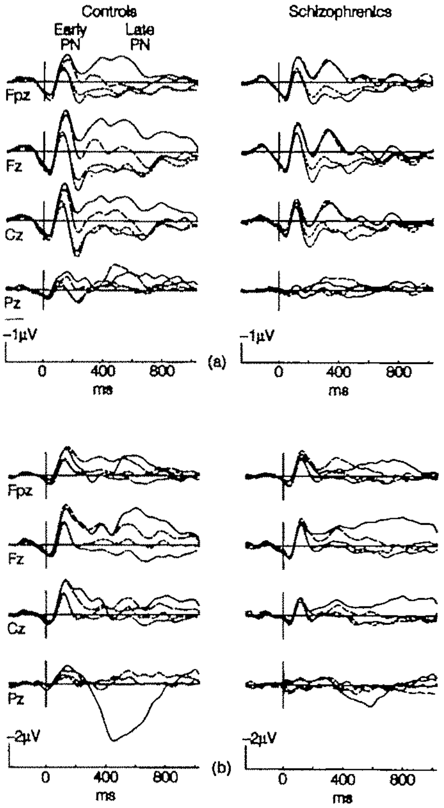

Fig. 1 Group mean ERPs recorded from midline scalp electrodes for ten unmedicated schizophrenic patients and ten healthy controls. ERPs were sorted according to whether or not stimuli matched the target on location (L+, L−) and pitch (P+, P−). (a) ERPs elicited by the short duration (D− or standard) stimuli. (b) ERPs elicited by the long duration (D+ or target) stimuli (L+P+, ———; L+P−, - - -; L−P+, ——; L−P−, -——-——) (negative potentials appear above the *x*-axis).

ERPs to targets

The P300 component, which was maximal for attended target (L+P+D+) stimuli at the parietal electrode in controls, was substantially smaller in schizophrenics (Fig. 1(b)). Both peak amplitude and mean amplitude at the Pz electrode were calculated within the 300–800 ms interval for ERPs elicited by correctly identified L+P+D+ stimuli. Both P300 amplitude measures were significantly reduced in schizophrenics compared with controls (mean (s.d.) peak amplitude: 2.31 (2.36) v. 5.24 (1.96) μV; $F(1,17)=8.80$, $P<0.01$; mean (s.d.) amplitude: 0.80 (2.27) v. 3.14 (1.52) μV; $F(1,17)=7.10$, $P<0.02$).

A substantial long-duration frontal negativity elicited by correctly detected target stimuli (L+P+D+) was apparent in both group grand means (see Fig. 1(b)). Mean amplitudes for the 400–1000 ms epoch at Fz were measured and did not differ significantly between patients and controls (2.07 (1.77) v. 1.96 (2.60)μV).

ERP measures and clinical ratings

Pearson correlations (one-tailed tests) were calculated between ERP measures and clinical ratings obtained from the SAPS and SANS. The amplitude of P300 at Pz was significantly correlated with negative thought disorder (the alogia score) ($r=-0.61$, $P<0.05$; Fig. 2), and the correlation with positive thought disorder approached significance ($r=-0.50$, $P=0.09$), but the amplitude of P300 was not significantly correlated with SAPS and SANS total scores after partialling out the correlations with ratings of thought disorder ($r=0.03$ for total negative symptoms and $r=0.13$ for positive symptoms).

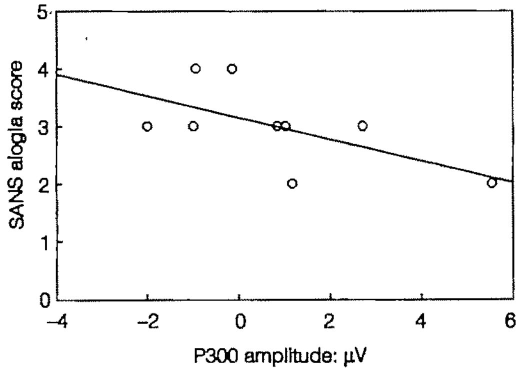

Fig. 2 SANS alogia score plotted against P300 amplitude at Pz ($r=-0.61$, $P<0.05$).

In contrast, early PN, measured at the Fz electrode as the difference between L+P+D− and L−P−D− ERPs, was significantly correlated with ratings of total positive ($r=-0.69$, $P<0.02$; Fig. 3) and negative ($r=-0.66$, $P<0.05$; Fig. 4) symptoms, and remained significant after partialling out correlations with ratings of thought disorder ($r=-0.69$ for total positive symptoms and $r=-0.72$ for total negative symptoms). A similar pattern of correlations was observed with the amplitude of late PN responses ($r=-0.77$, $P<0.005$ for total positive symptoms and $r=-0.81$, $P<0.005$ with total negative symptoms).

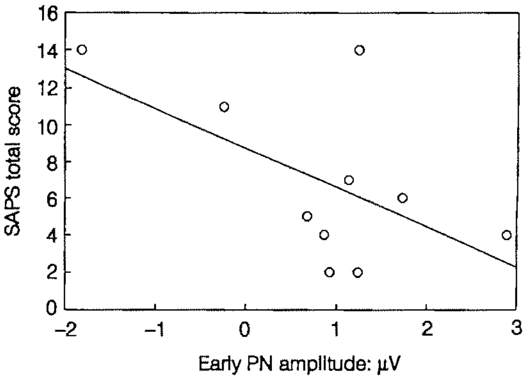

Fig. 3 SAPS total score plotted against early PN amplitude, measured as the difference between L+P+D− and L−P−D− ERPs at Fz ($r=-0.69$, $P<0.02$).

Discussion

The present study compared ERP indices of selective attention in unmedicated schizophrenics and healthy controls. As a psychiatric control group was not included, the group differences obtained in this study cannot be regarded as reflecting attentional deficits specific to schizophrenia. Investigation of patients with other psychiatric diagnoses using this task is currently being carried out in our laboratory.

By utilising a multidimensional selective listening task, we have shown that an early PN was present in both patients and controls, as reflected by significantly larger amplitudes to attended-location (L+) standards. Neither group showed any effect of pitch at the unattended location, suggesting that schizophrenics are capable of making a rapid selection on the basis of an easily discriminated feature (i.e. ear of delivery). This finding does not support the hypothesis that schizophrenics cannot ignore irrelevant stimuli, at

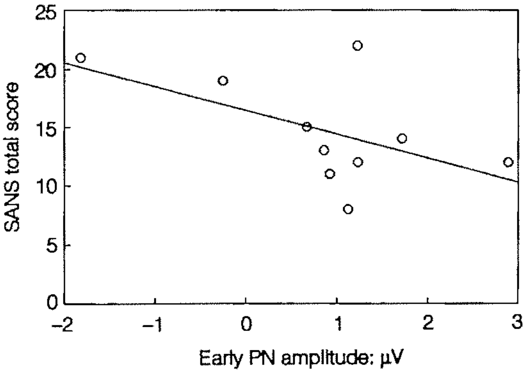

Fig. 4 SANS total score plotted against early PN amplitude, measured as the difference between L+P+D− and L−P−D− ERPs at Fz ($r=-0.66$, $P<0.05$).

least those that are easily distinguishable from relevant stimuli. The size of the early PN effect was significantly reduced at the vertex electrode site in schizophrenics as compared with healthy subjects, consistent with previous research using schizophrenics who were receiving antipsychotic medication (Baribeau-Braun *et al*, 1983; Hiramatsu *et al*, 1983). Kameyama *et al* (1987) failed to find a significant early PN effect in unmedicated schizophrenics. The latter finding may be related to the correlations obtained between PN amplitude and total scores for schizophrenic symptoms in the present study, such that patients with more severe symptoms had a smaller early PN amplitude. The schizophrenics in the study by Kameyama *et al* had higher mean total BPRS scores than the patients who participated in the present study (48.5 v. 37.8).

The present study also demonstrated significant reduction of P300 amplitude elicited by correctly detected target stimuli in unmedicated schizophrenic patients, and a significant association between reduced P300 amplitude and increased ratings of negative thought disorder (alogia). This finding is consistent with some previous studies which used other measures of thought disorder (Roth *et al*, 1979, 1980). In addition, we have previously reported a significant association between an object-sorting test of conceptual loosening and reduced P300 amplitude in two groups of psychiatrically healthy university students (Ward *et al*, 1984; 1991).

The present report provides the first evidence of marked attenuation of the late-PN component in schizophrenic patients. The significant early-PN effect and better than chance performance indicates that absence of late PN does not simply reflect schizophrenics' failure to engage in the task, or a general cognitive deficit. The virtual absence of late PN in schizophrenics cannot be attributed to inaccurate perception of stimulus characteristics, as EEG epochs contaminated by incorrect behavioural responses (misses or false alarms) were excluded from averaging.

Late PN in normals persisted well beyond the time at which correct button presses were usually made to the infrequent, long-duration 'targets'. This suggests that late PN reflects the maintenance of selective attention rather than perceptual and/or response-related processes. Naatanen (1982) has suggested that late PN reflects the process of updating or maintaining a sensory representation or 'attentional trace' for attended stimuli. The markedly reduced late-PN amplitude found in schizophrenics indicates that schizophrenic patients fail to maintain and direct the focus of attention, and the strong correlations between this ERP measure and ratings of total positive and negative symptoms, if replicated in future studies, would suggest a strong link between disability in information processing and schizophrenic symptoms.

The functional significance of the prolonged frontal negative potential found in both patients and controls for correctly detected target stimuli is not clear. If it can be regarded as evidence of differential pitch processing on the attended ear for long-duration stimuli, it indicates that schizophrenic patients distinguish these stimuli but, unlike normals, do not similarly process short-duration stimuli in the attended ear. This may indicate that patients utilise different strategies to controls in performing this complex listening task. Alternatively, the frontal negative potential elicited by correctly detected targets may reflect processes associated with response activation and resolution of motor activity, as these stimuli are the only ones that require a motor response.

The frontal-maximal group difference in late PN with the standards is consistent with neuropsychological test results indicating the importance of frontal-lobe structures for the maintenance of selective attention (Fuster, 1980). Although the frontal scalp distribution of late PN suggests the frontal lobe as a source of this activity, a study of patients with focal unilateral frontal lesions found bilateral reduction of PN amplitude (Knight *et al*, 1981). This finding is more consistent with subcortical generators receiving input from ipsilateral pre-frontal areas. The caudate nucleus has been suggested, as it receives projections from the frontal lobes and contains neurones involved in the maintenance of attention (Woods, 1990). The findings of the present study may thus be related to post-mortem (Seeman *et al*, 1984; Hess *et al*, 1987) and *in-vivo* (Crawley *et al*, 1986; Wong *et al*, 1986) evidence of neurochemical abnormalities in caudate and other striatal structures in schizophrenics.

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Unfit to Plead in England and Wales, 1976–88
A Survey

D. H. GRUBIN

The Home Office files of all 295 cases of defendants being found unfit to plead between 1976 and 1988 were evaluated. The majority were male and either schizophrenic or mentally impaired. Median age was 32 years. Two-thirds had past criminal convictions, and nearly 90% had past contact with psychiatric or social services, but only 28% were receiving psychiatric care at the time of their alleged offence; 14% were hospital in-patients. Offences of theft and violence predominated, but in most cases they were not of a serious nature: 34% were rated as mild or nuisance, 40% moderate, and 26% severe. In more than 80% of cases, evidence linking the accused with the offence seemed good. Less than one-third were admitted to special hospitals. Forty-six per cent of the population (135 patients) eventually regained their capacity to plead (within a median of four months), with 76 (26%) returning for trial. Of the remainder, 68 (23%) are still in hospital, 39 of whom have been there for more than five years. Time to discharge without trial reflected the severity of the alleged offence.

The procedure by which an individual is found unfit to plead in the UK, and the consequences that flow from such a decision, have been criticised frequently (Home Office & DHSS, 1975; Swan, 1981; Emmins, 1986; Chiswick, 1990). In particular, it has been observed that an individual who is found unfit to plead is deprived of his right to trial and faces possible life detention in hospital for a crime he was only alleged to have committed. However, little is known about those who have been found unfit to plead in Britain and discussion of the issues has taken place in a factual vacuum.

A person is found unfit to plead if he fails to satisfy criteria established in 1836 in the case of Pritchard, a deaf mute accused of bestiality. In essence, the defendant must be of sufficient intellect to make a proper defence. This has been interpreted as being able to plead to the indictment, to comprehend the details of evidence and the course of proceedings, and to know that a juror can be challenged. More recently, the ability to instruct legal advisers has also been included. The issue itself is decided by a jury, usually, but not necessarily, after the presentation of psychiatric evidence (Mitchell & Richardson, 1985).

Once found unfit to plead, an individual is dealt with under section 5 of the Criminal Procedure (Insanity) Act 1964 (CP(I)A), where the finding is referred to as "disability in bar of trial". The CP(I)A requires admission to hospital under conditions that are now equivalent to sections 37 and 41 of the Mental Health Act 1983 – that is, a hospital order with Home Office restrictions on discharge without limit of time. If the patient subsequently becomes fit to plead, the Act allows for remission back to court at the discretion of the Secretary of State; if the patient is not remitted for trial or does not become fit, he remains in hospital on the same footing as any patient under a restriction order, with discharge by the Home Secretary or a Mental Health Review Tribunal dependent on clinical and public-safety considerations.

Other than the occasional case description (Emmins, 1986), the research literature on unfitness to plead in England and Wales is limited to one study: a survey of psychiatric reports prepared at the time of trial for patients in an English special hospital (Larkin & Collins, 1989). If the net is extended to Scotland, only two further studies are found, one based on patients in a Scottish special hospital (Chiswick, 1978), the other a review of Scottish murder cases that eventually came back to trial (Normand, 1984). Even the number of people found unfit to plead in England and Wales is uncertain: the figures have not been published since 1980, and before 1980 there were frequent discrepancies between the data published by HMSO in *Criminal Statistics* and internal Home Office figures. In view of the important questions raised by a finding of unfit to plead in relation to the interaction between psychiatry and the law, it is surprising that more is not known about those found unfit to plead in Britain.

A number of studies in the US, however, have evaluated the equivalent finding of "incompetent to stand trial". In the 1960s, investigators noted that many patients found incompetent never left hospital. A Michigan survey, for instance, estimated that more than 50% of incompetent patients in a state hospital would never be released (Hess & Thomas, 1963), while a study in a Massachusetts hospital noted that before 1960 "more of this type of patient had left [the hospital] by dying than by all other avenues combined" (McGarry, 1971). In 1972, however, in *Jackson* v. *Indiana* (406 US 715), the situation changed when the US Supreme Court ruled that individuals incompetent to stand trial could not be held in hospital for an "unreasonable" length of time (Szasz, 1989). The effect has been that many more incompetent patients are now returned to court for trial, while those who remain incompetent are either detained on a civil (rather than a court) order, or they are released. Thus, by 1978 a national survey in the US found that the average length of stay in hospital for individuals incompetent to stand trial was approximately six months (Steadman *et al*, 1982).

In the UK, the legal situation is similar to that in America before the 1972 Supreme Court decision, in that there is no limit to the length of hospital detention or the duration of the order. It is not known, however, how long patients actually remain in hospital after a disability finding, what their psychiatric problems are, or how many return to court. As in America in the 1960s, it is possible for an individual to be detained in hospital without trial for the rest of his life, regardless of the nature or severity of his alleged crime.

This study is the first in-depth description of those found unfit to plead in England and Wales. It includes every individual known by the Home Office to have been found unfit to plead over the 13 years 1976–88.

Method

C3 division of the Home Office kindly provided access to its files on all individuals found unfit to plead in England and Wales between 1976 and 1988 inclusive. Each file commenced at the time the Home Office was informed by a crown court of an unfitness finding. The files included the background needed to find a suitable hospital for a patient, and grew as the patient was monitored in hospital. The files contained a description of the alleged crime supplied by the police, the patient's antecedents and criminal record, contemporary psychiatric reports, regular progress reports by the responsible medical officer (RMO), notes on Home Office thinking about the case, and relevant correspondence. In cases where the files were incomplete, an attempt was made to obtain further information from the hospital where the patient was sent, or from the court.

Each file was evaluated with a prepared check-list. Information was recorded about personal background, psychiatric history, the alleged offence, mental state, treatment, and outcome. September 1989 was the last month for which follow-up information was obtained; where a file was reviewed early in 1989 and a change in status was a possibility, an update was obtained in September from the case worker involved.

Results

From 1976 to 1988 there were 295 findings of unfitness to plead in England and Wales documented by the Home Office (Fig. 1). This figure is a slight under-representation of the actual number of unfit findings because the Home Office

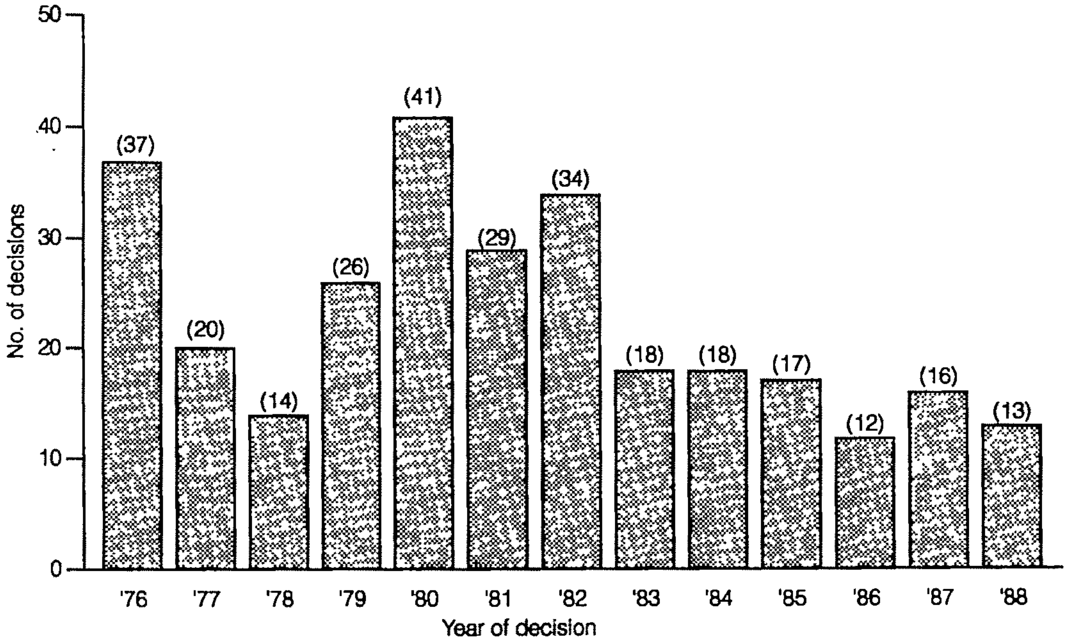

Fig. 1 Number of findings of unfit to plead, each year, 1976–88.

no longer retained information on a very small number of cases (six at most) from the years 1976–79 where a hospital could not be found that was willing to take a patient and it was not thought necessary because of the trivial nature of the case to direct admission against a hospital's wishes. In those cases the individual was released from prison after the two-month holding period allowed by the Act, and Home Office interest in the case ended. From 1980, information about even this unusual type of case was available.

It can be seen from Fig. 1 that the number of findings has declined steadily over the last decade. The mean number per year for the entire 13 years is 22.7; however, for the first seven years, the mean is 28.7, while over the next six years the mean falls to just 15.7, a significant decrease ($t = 3.47$, $P < 0.01$). The reason for this drop in findings is unclear, although it should be noted that it becomes most pronounced in 1983, before the Mental Health Act 1983 came into force; the decline in fact continues a trend which began in the late 1940s (Walker, 1968).

Over the years of the survey, seven people were found unfit to plead on two occasions, and one on three occasions (one man who appeared twice in this survey was also found unfit to plead twice in the early 1970s, giving him a possible record of four findings of unfit to plead). The 295 cases thus involved 286 individuals.

Table 1
Characteristics of those found unfit to plead ($n = 286$)

	No.	%
Criminal background		
No previous convictions	92	32.2
Non-violent convictions only	145	50.7
Violent convictions	44	15.4
Unknown	5	1.7
Past prison sentences	88	30.8
Past hospital orders	59	20.6
Psychiatric background		
Past contact with services	250	87.4
Past hospital admission	221	77.3
Admission on (civil) section	101	35.3
Unfit to plead (pre-1976)	9	3.1
In contact with services at time of offence[1]	82	27.8
In-patient at time of offence[1]	42	14.2
Default from contact within six months of offence[1]	34	11.5
Primary diagnoses		
Schizophrenia	170	57.6
Other psychosis	26	8.8
Dementia	10	3.4
Personality disorder/neurotic disorder	11	3.7
Mental handicap/brain damage	68	23.1
Deaf	7	2.4
None	3	1.0

1. Relates to the 295 cases in which the population was involved.

The population

Of the 286 individuals comprising the sample, 88% were male. The sex distribution was similar to that appearing before the crown courts over these years, which was approximately 86% male (*Criminal Statistics*, 1976–88).

The mean age of the population was 35.7 years (s.d. 14.4, range 16–86 years), and the median age was 32. Although women had a higher mean age (40.0 compared with 35.1 for men), the difference was not significant. Age norms for the crown court population over the years of the survey are not known, but as half of indictable offences are committed by males less than 21 years of age (Walker, 1987), it can be assumed that those found unfit to plead are an older group.

Three-quarters of the population were Caucasian; of these, 9% were born outside the UK and Ireland. Most of the remaining cases were of Caribbean descent (15%), the majority of whom (75%) were born outside the UK. Overall, 27% of those found unfit to plead were born outside the UK.

A criminal record was possessed by 189 (Table 1) or two-thirds of the population; 31% had served prison sentences and 21% had received a hospital order from the courts in the past.

Nearly 90% had had past contact with psychiatric services or, in the case of mental handicap, social services; over three-quarters had a history of hospital admission, and over a third had been in hospital under a civil section of the Mental Health Act. However, in many fewer cases (28%) were individuals receiving psychiatric care at the time of the alleged offence, although a further 12% had defaulted from care in the previous six months (these were almost all mentally ill rather than mentally handicapped). Forty-two individuals were in-patients at the time, 20 of whom were mentally handicapped. Of the 179 who had a history of hospital admission but were not currently in-patients, the median number of months since their most recent discharge was 13.

A diagnosis was reached in each case based on all of the available medical reports. In cases where a patient had more than one diagnosis, the one that appeared to be most responsible for the unfitness finding was counted as primary. In a case of schizophrenia and mental handicap, for instance, a diagnosis of schizophrenia was given if the patient was psychotic at the trial and it was the psychosis that rendered him unfit.

More than half the population had a primary diagnosis of schizophrenia; and a further 23% were primarily mentally handicapped or brain damaged. Nineteen others also suffered from mental handicap or brain damage, but were found unfit for other reasons (usually a concurrent psychotic illness). In total, therefore, about 30% had some degree of mental handicap or brain damage, and more than 80% of the population were schizophrenic, mentally handicapped, or brain damaged.

When present, mental handicap was often not severe, at least if IQ is used as an indicator: 32% had IQs between 60 and 70, and 38% between 50 and 60.

Just seven findings involved individuals who were profoundly deaf and unable to communicate – the classic 19th-century cause of an unfitness finding. In only one of these cases was a mental illness also thought to be present. For the purposes of the Mental Health Act, these patients were usually classified as mentally impaired.

Table 2
Type of offence and level of severity

	No. (%)	% nuisance	% mild	% moderate	% severe
Theft/fraud	79 (27%)	32	42	27	0
Property damage	7 (2%)	57	29	14	0
Violence	92 (31%)	1	21	48	30
Homicide	28 (9%)	0	0	0	100
Possession of weapon	7 (2%)	14	14	57	14
Assault on police	11 (4%)	9	46	46	0
Sex offence[1]	31 (11%)	3	10	67	20
Arson	33 (11%)	0	3	58	39
Other	7 (2%)	29	14	57	0
Total	295	12	22	40	26

1. No information was available about the severity of the crime on one sex offence.

The offence

Many individuals were charged with more than one offence. For analysis, only the most serious charge was considered (Table 2). The most common type of offence was that of violence, accounting for 41% of the total: 28 homicide and 92 lesser assaults. The next most frequent offence type was theft and fraud. Seventeen per cent of the alleged offences were against family members.

Offence type alone, however, means little. Violent crimes, for instance, range from minor assault to homicide. Offences were therefore rated according to their severity (Table 2). *Nuisance* offences were those in which there was no physical risk and any property involved was of negligible worth (under £10 in value) – for instance, stealing milk bottles from a doorstep, or breaking into a conservatory to sleep. *Mild* offences were those in which any violence was minor or property was valued under £50 – for instance, refusing to pay a taxi fare, or punching out at a family member. *Moderate* offences were those in which some injury could have or did occur but which was not serious, or any property involved was valued up to a few thousand pounds – for instance, stealing a car or threatening a police officer with a knife (although not actually injuring him). *Severe* offences were those in which there was a substantial risk of physical injury or severe injury occurred, or property value was substantial.

It can be seen from Table 2 that offences rated severe accounted for about a quarter of the total, while nuisance and mild offences together accounted for more than a third. Excluding homicide, the majority of violent offences were not of a severe nature, and about one-fifth were rated as nuisance or mild. Interestingly, although individuals of no fixed abode formed about a quarter of the sample, they accounted for 54% of the nuisance offences, significantly more than expected by chance ($\chi^2 = 14.52$, $P < 0.001$).

The judicial process

The quality of evidence against the accused was rated as clear or unclear based on the following criteria: presence of an eye witness; evidence found on the accused; forensic evidence linking the accused with the act; or a clear confession that was neither retracted nor challenged by the defence. In spite of the relatively limited amount of information about the offence in the files, the accused seemed to be clearly implicated in 83% of cases; frequently the accused was arrested at the scene of the crime.

In about 70% of cases there was a comment in the file by the accused regarding his/her guilt or innocence; in 8% of these cases statements were contradictory or unclear, in 68% the accused admitted the charges, while in 24% the accused denied them, although often for psychotic reasons. For instance, one man accused of seriously wounding his parents admitted the act but denied his guilt because he said his acts were controlled by laser beams from outer space. There is special worry about confessions in relation to the mentally handicapped, but in this survey there were only seven cases where mentally handicapped individuals found unfit to plead had confessed to offences where, given the available information, the evidence linking them to the offence was less than clear.

The most common findings in the mental state were paranoid ideas or delusions, and thought disorder. Hallucinations were described in about a third of cases. Disorders of affect as a primary finding (that is, not in association with schizophrenia) were relatively uncommon. Amnesia was mentioned in 14 cases, but seemed to be the prime reason for the psychiatric recommendation in just two.

Reasons given by psychiatrists and prison medical officers in written reports for recommending that an individual be found unfit to plead are somewhat beside the point, as oral evidence led by a barrister is almost always given in court. The reports, however, do give an indication of the psychiatric thinking behind a recommendation of unfitness. The three most popular criteria mentioned in the reports were: being unable to instruct legal advisers (195 mentions), being unable to comprehend court proceedings (144 mentions), and being unable to challenge a juror (98 mentions). Other reasons included lacking insight into delusional thinking, and being unable to appreciate the imposition of a sentence. In one case of mental handicap an unfitness finding was recommended because the man involved was said to be "often not truthful . . . and his statements would be misleading". In some cases there was obvious confusion with the insanity criteria of being unable to distinguish between right and wrong.

Outcome

The majority of patients were sent to local psychiatric hospitals; under one-third were sent to one of the maximum-security special hospitals (Table 3). In a small number of cases patients were sent to a special hospital not on security or clinical grounds, but because the catchment-area hospital refused admission. Nine individuals were not admitted to hospital: six were declared fit while still in prison and were returned directly to trial, and three were simply discharged from prison.

Table 3
Hospital disposal

	No.	%
Local	170	57.6
Regional secure unit[1]	21	7.1
Special hospital	88	29.8
Private	7	2.4
None	9	3.1

1. Regional secure units were not in existence in the early years of the survey.

Once the patient is in hospital, the RMO alone determines whether or not he/she remains unfit to plead, and advises the Home Secretary accordingly. In total, 135 patients (46%) were declared fit to plead by their RMO, and 160 (54%) remained unfit. In 56 cases within the unfit group, however, the RMO was not asked to comment specifically on fitness, but it seemed likely from medical or tribunal reports that the patient had in fact become fit to plead (only in the last few years has the Home Office routinely inquired about a patient's fitness status; previously the issue tended to be raised only if a trial was being considered, or if a relatively early discharge was requested). In 22% of cases where the primary diagnosis was mental handicap or brain damage, the individual recovered his/her capacity to plead, and in another 12% this seemed likely; thus, in more than a third of cases of mental handicap or brain damage, where a change in fitness status should be unlikely, fitness was in fact regained.

In the 135 cases in which individuals became fit to plead, the average time between the initial finding and the RMO advising the Home Office that the patient had become fit was 10.5 months. However, the range in time was large, from nil (for instance, in cases where the admitting doctor disagreed with the finding) to nearly 12 years. The median time between the finding and eventual fitness, probably a more meaningful figure than the mean in view of the skewed distribution, was four months; 82% of those who became fit did so within a year. These figures, of course, are an overestimate of the time taken to regain capacity to plead as there is almost always a delay between a patient being considered to have become fit and the Home Office being informed by the RMO.

Outcome for those who regained fitness is shown in Table 4. It can be seen that the majority returned to court, while just over 10% are still in hospital. Those remaining in hospital in spite of becoming fit to plead have been detained for an average of 5.4 years since the original finding. Forty-three patients (excluding one patient who died in hospital) were discharged from the conditions of the Act without returning to court – this group was detained for a mean of 30 months (s.d. 36.5), and a median of 15 months.

Outcome in the 160 cases where fitness was not regained is also illustrated in Table 4. Patients in hospital who have not become fit to plead have been there for an average of 6.2 years since the original finding; 4 have been in hospital 12 years, 11 for more than 10 years, and 39 for more than 5 years.

For those patients who never became fit to plead but were anyway discharged, the mean time detained was 35 months, with a median of 23 months. Time to discharge reflected severity of offence, with those accused of nuisance or mild offences discharged after an average of 26 months, those accused of moderate offences after 40 months, and those accused of severe offences after 55 months ($F=15.05$, $P<0.001$).

In the subgroup of 56 patients who were not formally declared fit to plead but who probably became so, 12 (21%) are still in hospital, the average length of detention since the decision being 7.2 years.

Table 4 also provides a summary of outcome for the entire population. It can be seen that about a quarter returned to court and a quarter are still in hospital (because one man was found unfit to plead on two subsequent occasions for new offences without ever leaving hospital, the 70 cases represent 68 individuals); a small number of patients died while detained as unfit to plead. Two of those still detained have court cases pending (and in fact have since appeared in court in early 1990). Five patients have been in hospital for 12 years (the maximum possible in this survey), 12 for more than 10 years, and 47 for more than 5 years. Of the 212 patients who left hospital (either discharged or returned to court) and excluding those who died, 118 (56%) did so within one year, and 150 (71%) within two years.

Trial

Before 1982, Home Office policy was to remit to court only if there were exceptional reasons to do so; after this date the policy was altered so that failure to remit, rather than remission, had to be justified. The effect of this policy change can be seen in Table 5: the proportion of individuals returning to court increased substantially in the 1980s – before 1982, 20 of 167 (12.0%) returned for trial; after 1982, 56 of 128 (43.8%) returned ($\chi^2=38.25$, $P<0.001$).

The mean length of time between original finding and eventual appearance in court was 14 months (range 3 months to 8½ years – two trials took place more than 8 years after the initial finding); the median was 10 months. Five individuals who returned for trial were found not guilty, and another five had their cases left on file or no evidence was offered; in the remaining 66 cases a guilty verdict was returned. Ten of those found guilty received prison sentences, 38 received hospital orders (25 with restrictions) and 18 were given non-custodial sentences such as probation orders or suspended sentences.

There were various reasons why someone who became fit was not remitted for trial. Most common were the length of time that had passed since the original offence and the

Table 4
Outcome

	Remained unfit	Became fit	Total
Remains in hospital[1]	53 (33.5%)	15 (11.1%)	68 (23.2%)
Conditional discharge	31 (19.6%)	23 (17.0%)	54 (18.4%)
Absolute discharge	7 (4.4%)	4 (3.0%)	11 (3.8%)
Restrictions lifted	51 (32.2%)	14 (10.4%)	65 (22.2%)
Death	12 (7.6%)	1 (0.7%)	13 (4.4%)
Trial	0 (0.0%)	76 (56.2%)	76 (25.9%)
Other	4 (2.5%)	2 (1.5%)	6 (2.0%)
Total	158 (53.9%)	135 (46.1%)	293

1. One individual who was found unfit on two further occasions while still detained on the original finding and who remains in hospital has only been counted once.

minor nature of the offence (if the patient insisted on his right to trial, however, Home Office policy was to remit if possible). Even given the bias against remitting for minor offences, 23% of subsequent trials involved nuisance or mild offences.

Thirteen patients died in hospital while still detained as unfit to plead. Six were patients with senile dementia, two were patients with probable alcoholic brain damage, and two were elderly schizophrenic patients. Three of the younger schizophrenic patients died, all within one year of the finding: two were by suicide and one was from an unknown cause.

Since the Mental Health Act 1983, tribunals have had the power to discharge patients under restriction orders (including those held under the CP(I)A). Tribunals, however, are not empowered to rule on whether the patient has become fit to plead. By September 1989, tribunals had discharged 25 patients found unfit to plead, 22 conditionally and 3 absolutely. Of these 25 patients, 7 had been accused of offences rated severe, and 12 of offences of moderate severity; in 23 of these cases, the evidence linking the individual to the offence seemed clear. Eleven of the patients released by tribunals had been declared fit by their RMO, and a further seven were probably fit at the time of their tribunal hearing.

Table 5
Number coming to trial

Year of decision	Number of findings	Number coming to trial
1976	37	5 (13%)
1977	20	2 (10%)
1978	14	2 (14%)
1979	26	3 (11%)
1980	41	4 (10%)
1981	29	4 (14%)
1982	34	17 (50%)
1983	18	7 (39%)
1984	18	5 (28%)
1985	17	5 (29%)
1986	12	7 (58%)
1987	16	9 (56%)
1988	13	6 (46%)

Discussion

The concept of fitness to plead is associated with the principle of a fair trial, but its origins lie in the rituals of the medieval court of law – without the opening plea the trial could not take place (Hibbert, 1963; Walker, 1968). The idea as we know it did not take shape until the 19th century, evolving through case law mainly in the context of deaf mutes, some of whom may have been mentally defective as well. Today, it is primarily the mentally ill who are pulled into its orbit, and although it is a jury that makes the final decision, it is the psychiatrist who almost always makes the crucial recommendation. The question is, are psychiatrists acting in their client/patient's best interests when they recommend a finding of unfit to plead, or are they, with the best of intentions, using an archaic legal philosophy which in the end does more harm than good?

A finding of unfitness to plead is meant to protect an individual from trial if his mental state mitigates against the possibility of the trial being fair. During the course of the survey it became apparent that many individuals who are found unfit to plead seemed little different from the majority of mentally disturbed or mentally handicapped defendants who come before the courts every year – indeed, two-thirds of the population had been dealt with previously by the courts in a normal manner. Although it is possible that on earlier occasions a different mental state was evident, on the whole this population was not a stranger to court proceedings. It was of interest that while mentally handicapped and brain-damaged individuals accounted for about 23% of the population found unfit to plead in England and Wales, they are not commonly found incompetent to stand trial in America (Lamb, 1987; Reich & Wells, 1986).

From the information available it was often not possible to determine with certainty who first raised the issue of fitness to plead, but it appeared that the prosecution was the prime mover in 35% of findings. Only rarely was this challenged by the defence. The defence itself seemed responsible in about a third of cases, and in another third both prosecution and defence seemed equally involved in the early stages. Occasionally it was the judge who first questioned the defendant's fitness to plead. On occasions the issue was raised as an expediency. A mentally ill defendant who threatens the 'dignity of the court', for example, can be found in contempt, but the apparently more humane CP(I)A may be used instead; this was particularly true when psychotic individuals insisted on representing themselves in court without legal assistance. In other cases, prison medical officers would recommend a finding of unfitness not because they believed that the accused was unfit to plead, but because they had been unable to find a psychiatric bed in any other way; once the unfitness decision was made, responsibility for finding a bed shifted to the Home Office, which could direct admission to a named hospital if all else failed. However, it would require a prospective study to understand why particular individuals are singled out to travel the unfitness pathway when so many others like them are thought able to stand trial.

There are certainly a number of serious problems which arise from the use of the CP(I)A. A law that is meant to protect vulnerable individuals has had the unintentional consequence of entrapping them in a nether world between criminality and mental illness, where the psychiatrist becomes the primary gatekeeper to any return to court, and where the Home Office must oversee the management of patients who may or may not have committed a crime and whose condition may or may not justify the imposition of restrictions. But the fault does not lie solely in the CP(I)A: in many cases there seemed little need to find individuals unfit to plead at all. Those who unequivocally benefited were the substantial minority for whom guilt was unclear and the trial delay allowed for an improvement in their mental state. The rest had their long-term management delayed at best, and at worst risked indefinite detention in hospital.

There are two areas which are in particular need of review: the way in which judgements about fitness capacity are reached, and the length of time restrictions remain in force.

Judgements

In 1975 the Butler Committee (Home Office & DHSS, 1975) comprehensively reviewed the law in respect to disability in relation to trial (its preferred terminology). Among other things, it recommended that in cases where recovery was likely the trial should be adjourned for up to six months to allow treatment to be given, and that if there is no recovery a trial of facts should take place.

Certainly the speed with which mentally ill individuals recovered their fitness once they received treatment in hospital was impressive – if fitness was going to be regained, it was usually done so within a few months. Although it was difficult to judge how often appropriate drug treatment was initiated in prison or pre-trial transfer to hospital attempted, 80% of the population had their full assessment in prison, where circumstances might be thought to be less conducive to recovery. A mandatory treatment period as suggested by the Butler Committee would have drastically reduced the number of unfitness findings over this period.

Curiously, the Butler Committee was satisfied that in most cases there was little doubt about whether an individual was under disability or not. But unfitness to plead is not an objective fact about a person. In this survey, although disagreement between psychiatrists was not always readily apparent because of variations in patients' mental state at the time of their different reports, disagreement about fitness status was clear in about 15% of cases, a figure similar to that found in some American studies (Phillips *et al*, 1988).

Whether or not there is psychiatric disagreement, the criteria used to judge fitness are extremely flexible, and are used idiosyncratically and arbitrarily. This partly explains why fitness is so commonly restored in the mentally handicapped, for whom recovery should be rare. For example, one mentally handicapped man with 11 previous convictions was found unfit to plead to a charge of robbery. After his conditional discharge four years later, he appeared in court on four separate occasions, and was convicted each time, with no apparent change in mental state and while technically unfit to plead to the original charge. The arbitrary use of the fitness criteria can also be seen in the case of a schizophrenic man who was found unfit to plead in 1978 to a charge of murdering his baby nephew. He admitted the killing to the police and to various psychiatrists, saying that "the baby is always getting me into trouble so I hit it". The psychiatrist who recommended the unfitness finding wrote that the accused felt "he was being brainwashed and that people were out to lock him up . . . in my opinion he is clearly unfit to instruct solicitors or to plead to the present charges". When seen by a Mental Health Review Tribunal the following year, his solicitors and the tribunal both believed he was fit to stand trial. The RMO disagreed, and that decision was final. Subsequent tribunals and independent psychiatrists continued to state that the patient was fit, but it was not until a change in RMO in 1984 that he was officially declared fit to plead. He eventually went to trial in 1986, eight years after the initial decision, when he was found guilty of manslaughter. In both these cases, different interpretations of what it means to be fit to plead, rather than anything about the individual's mental state, determined fitness status.

Psychiatrists also commonly stated that an individual was unfit to plead if suffering from paranoid delusions. For instance, one psychiatrist recommended that a man who failed to pay a taxi fare should be found unfit because "he believes he has the right to summons a taxi without paying and that he has the right to confiscate the taxi if the driver refused to accommodate him. It is on these grounds that he would plead not guilty"; in another case in which a man was accused of murdering his father, the psychiatrist wrote, "He believes he was acting under instruction and control by another agency and would consider, therefore, that the principal witnesses in trial should be from the Secret Service and members of Government as he believes that they can exonerate him. . . . His view of court procedures therefore is completely distorted by schizophrenic illness". In both these examples, the defendant admitted the offence but provided reasons why he should be considered not guilty. But it should be up to judge and jury, not psychiatrist, to decide on the merits of the defence. In fact, in the case of *R.* v. *Robertson* (1968, 52 CrAppR 557-560), a man with paranoid delusions, the Court of Appeal ruled just that, stating, "the mere fact that the appellant was not capable of doing things which were in his own best interests was insufficient ground for a jury to return a finding of disability". This ruling, however, did not always seem to be followed by the lower courts. There were at least 20 cases of individuals found unfit to plead solely on the basis of a paranoid mental state, and a number of other cases in which it played an important role.

Length of restrictions

Perhaps the most disturbing finding of this study was the fact that nearly a quarter of those found unfit to plead between 1976 and 1988 remain in hospital under the CP(I)A; a further 11%, although conditionally discharged, are still subject to the Act and remain liable to recall. On the whole, those still in the shadow of the Act tend to be more disturbed and in need of more prolonged treatment – an in-depth analysis of this group is the subject of another report (Grubin, 1991). But it should be remembered that the purpose of restrictions in the CP(I)A is to ensure that the accused can be brought back to trial; restrictions do not relate to either security or clinical considerations. In theory, therefore, if a trial is not to take place, the restrictions should be removed. However, there is often an understandable reluctance by the Home Office to do this, particularly when the alleged offence is serious or reports on the patient are worrying. Unfortunately, this can sometimes result in confusion as to whether an individual is a patient or a criminal.

One way around this problem would be to follow the course taken in America, where an individual found incompetent to stand trial can be held in hospital for a limited period only. The problem with this approach is that it may then become positively advantageous to be found unfit. Steadman *et al* (1982), for instance, estimated that in the US there are three to four admissions to hospital for a competency evaluation for every positive finding; in one report, positive recommendations were made in only 2 of 87 cases admitted for evaluation (Geller & Lister, 1978). Although the guaranteed lifting of restrictions prevents lengthy detention without trial, it is far from clear that the delay in trial caused by an increase in fitness evaluations would act in an individual's interests, or that a rise in unfitness findings would be a step in the right direction.

The Butler Committee's recommendation of a trial of facts if recovery of fitness does not occur within six months is intended to protect those who are not guilty. In this survey, however, the problem was instead that in more than 80% of cases there seemed little doubt that the individual had committed the alleged offence. In those cases, the trial delay and lack of long-term disposal served little purpose, and made management more difficult: the legal proceedings remained unresolved, the Home Office became involved in cases that represented little risk to public safety, and rehabilitation plans were impeded. Unless the judge is granted options in disposal in place of the current mandatory hospital order with restrictions (a further Butler recommendation), merely settling guilt at a trial of facts would serve little purpose.

Recommendations for change

In order to overcome the difficulties outlined above, the following recommendations for change are suggested.

(a) The decision of whether an individual is fit to plead or not should be taken by the judge, not a jury, either on his/her own initiative or at the request of the defence. The prosecution should no longer be able to raise the issue.

(b) A finding of unfit to plead should be made by the judge only if a conviction is thought to be unsafe in view of the defendant's mental state. An individual would be found unfit to plead where the defence planned to contest the case, and where an improvement in mental state would materially influence the outcome.

(c) Only one criterion should be retained: whether or not the ability of the defendant to instruct his legal representatives is significantly handicapped by mental illness or mental impairment. The psychiatrist's role would then be to give an opinion on the presence and severity of any mental illness or mental impairment, and the likely prognosis. This would be more in keeping with the spirit of the concept, which is that any trial should be a fair one. It would be up to the court to decide the legal issue of fitness.

(d) Psychiatrists should give an opinion on the mental state of the individual and prognosis only; they should not be asked to comment on issues of fitness to plead.

(e) Following a ruling of unfit to plead, the judge should determine how long restrictions will remain in force, depending on the nature of the alleged offence and the amount of time beyond which a trial would be inappropriate. In cases where the alleged crime was serious, for instance, restrictions would last indefinitely; in less serious cases, restrictions would last for a limited period, or no further appearance in court might be thought necessary at all, and a disposal without restrictions would follow.

(f) After admission to hospital, fitness status should be regularly reviewed by Mental Health Review Tribunals, and the decision of whether fitness has been regained should be made by the tribunal, not the RMO.

(g) The feasibility of a trial being mounted should be regularly reviewed. Regardless of whether fitness has been regained, if a trial is no longer felt possible or desirable, the patient would no longer be viewed as unfit to plead. Instead, the patient should be referred to a Mental Health Review Tribunal to determine whether restrictions need to remain in force.

Conclusion

Being unfit to plead is not a psychiatric condition – it is a legal concept. The criteria relate to intellectual functioning only, and reflect 19th-century views of legal insanity. For better or worse, psychiatrists have become intrinsically involved in the process. Their recommendations, by necessity, have more to do with philosophy than psychiatry. Whether psychiatrists make good legal philosophers is open to debate.

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Prevalence of Delusional Jealousy in Different Psychiatric Disorders

An Analysis of 93 Cases

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The prevalence of delusional jealousy in 8134 psychiatric in-patients was 1.1%. Delusions of jealousy were most frequent in organic psychoses (7.0%), paranoid disorders (6.7%), alcohol psychosis (5.6%) and schizophrenia (2.5%), while in affective disorder delusions of jealousy could be found in only 0.1%. Because schizophrenia and affective disorder were the most common diagnoses, most patients with delusions of jealousy were schizophrenics. In schizophrenia, women were more likely to suffer from delusional jealousy, while in alcohol psychosis, men were more likely than women to suffer from delusional jealousy.

As Bishay *et al* (1989) pointed out, the term 'morbid jealousy' has been used to describe a wide range of phenomena, including delusional states as well as jealous reactions in different psychiatric groups. The nomenclature is confusing: the terms 'morbid jealousy' (Vauhkonen, 1968; Docherty & Ellis, 1976) 'sexual', 'pathological' or 'psychotic' jealousy (Tiggelaar, 1956; Munro, 1984), 'erotic jealousy syndrome' or 'Othello syndrome' (Todd & Dewhurst, 1955; Langfeldt, 1961) all have been proposed to describe delusions of infidelity. Enoch & Trethowan (1979) proposed that the term 'Othello syndrome' be used if delusions of infidelity "occur in pure form". The terms 'morbid' or 'obsessional' jealousy are sometimes used to categorise neurotic, non-delusional forms of jealousy. In this article we report only on cases with delusional, psychotic jealousy.

In the 19th century, delusional jealousy was first described in alcoholics. Krafft-Ebing (1891) found jealous ideas in 80% of all male alcoholics and believed it to be pathognomonic for alcoholism. Delusional jealousy is a symptom not only described in alcoholism (Kolle, 1932; Llopsis, 1962; Postrach, 1988) but also in schizophrenia, organic psychoses and paranoid disorders (Liebers, 1919; Gausebeck, 1928; Scholz, 1930; Ortega, 1959; Shepherd, 1961; Retterstol, 1967).

Delusional jealousy is difficult to diagnose. Apart from both patients and the spouses being reluctant to talk about it, it is difficult to verify or exclude infidelity of the spouse. A patient may suffer from delusions of jealousy even when the spouse's infidelity has been verified (Jaspers, 1910) – a severe problem for the diagnostic classification as delusional (Spitzer, 1989). While there is some literature on the psychology of delusional jealousy (Scholz, 1930; Hahn, 1933; Marcuse, 1950; Wendt, 1951; Tellenbach, 1967; Docherty & Ellis, 1976; Pauleikhoff, 1977), there is little information on the prevalence rate in different psychiatric conditions and on the possible influence of age and sex in the development of the syndrome.

The following study was conducted to examine:

(a) the prevalence of delusional jealousy in different psychiatric disorders and
(b) the possible influence of age and sex on the aetiology of delusional jealousy.

Method

In a retrospective study the case histories of *all* in-patients who had been treated in the Psychiatric Hospital of the University of Munich between 1981 and 1985 were examined. The World Health Organization's (1978) ICD-9 criteria were used for diagnosis. Besides the case histories, relevant demographic data, past psychiatric history, the psychiatric family history and especially psychopathology had been documented by means of the AMDP system (Guy & Ban, 1982). Among the different psychopathological symptoms, 'delusions of jealousy' is listed as item number 41 and defined as "conviction of being deceived or betrayed by loved ones. An unfounded conviction". Psychopathology has been documented both on admission and discharge.

Results

There were 8134 psychiatric in-patients (mean age 41.8 years), 55.6% of whom were women (mean age 44.5 years, male mean age 37.7 years). Ninety-three subjects with delusional jealousy were identified. The overall prevalence rate was thus 1.1%. Delusions of jealousy were commonly documented in: organic psychosis (prevalence rate 7.0%), paranoid disorders (6.7%), alcohol psychosis (5.6%) and schizophrenia (2.5%), and, very infrequently, in patients with affective disorders (0.1%) and neuroses or psychopathy (0.6%) (Table 1).

For further statistical analyses, only the 6041 patients classified by one of these above diagnoses were taken into account.

Table 1
Relationship of delusions of jealousy to diagnosis, age and sex

ICD-9 code	Diagnosis	Numbers	Mean age years	No. of men	Mean age: years	No. of women	Mean age: years	Female: male ratio
All patients		6041	41.8	2452	37.7	3589	44.5	
With delusional jealousy		93	41.6	42	39.5	51	42.3	
290	Organic psychosis	86	70.4	36 (41.8%)	70.5	50 (58.2%)	70.3	1.38:1
	With delusions of jealousy	6	55.0	3 (50%)	44.7	3 (50%)	65.3	1:1
291	Alcohol psychosis	198	40.6	142 (71.7%)	40.5	56 (28.3%)	40.7	0.39:1
	With delusions of jealousy	11	45.0	10 (90.9%)	45.7	1 (9.1%)	43.0	0.1:1*
295	Schizophrenia	2084	34.7	864 (41.4%)	31.3	1220 (58.6%)	36.8	1.41:1
	With delusions of jealousy	52[1]	38.1	16 (30.7%)	34.7	36 (69.3%)	39.0	2.25:1*
296	Affective psychosis	2086	50.1	644 (30.8%)	45.2	1442 (69.2%)	52.3	2.17:1
	With delusions of jealousy	3	47.0	2 (66.7%)	52.0	1 (33.3%)	37.0	0.5:1[2]
297	Paranoid syndrome	195	51.5	53 (27.1%)	43.0	142 (72.9%)	54.4	2.67:1
	With delusions of jealousy	13	48.2	6 (46.1%)	42.0	7 (53.9%)	52.3	1.16:1[2]
298	Other psychosis, non-organic	84	35.4	28 (33.3%)	32.8	56 (66.7%)	36.9	
	With delusions of jealousy	2	33.5	1 (50%)	26.0	1 (50%)	41.0	
300	Neurosis	519	38.9	241 (46.6%)	38.1	278 (53.4%)	38.9	
	With delusions of jealousy	3	32.0	2 (66.7%)	30.5	1 (33.3%)	35.0	
301	Personality disorders	250	34.3	146 (58.4%)	33.7	104 (41.6%)	35.1	
	With delusions of jealousy	2	45.5	2 (100%)	45.5	0	0	
309	Psychogenic reaction	539	37.4	298 (55.2%)	36.2	241 (44.8%)	39.3	
	With delusions of jealousy	1	41.6	0	-	1 (100%)	42.3	

1. In two cases associated with alcohol abuse/dependence.
2. No statistical analysis performed as numbers are too small.
$^*P<0.01$ (χ^2).

With respect to absolute figures, six of the 86 patients with organic psychosis suffered from delusions of jealousy – two with senile dementia or drug-induced psychosis, one patient with encephalitis and subarachnoid haemorrhage. Thirteen of the 195 patients with paranoid syndromes and 52 of the 2084 patients with schizophrenia had delusions of jealousy. Among the 52 schizophrenics, 24 were diagnosed as paranoid type and 21 as schizoaffective. With respect to alcohol psychosis, 11 of the 198 patients had these delusional symptoms, of whom four had a pure, 'monosymptomatic' delusional syndrome, the remaining seven displaying additional hallucinatory or delirious symptoms. Only three of the 2086 individuals with affective disorder reported delusions of jealousy.

With respect to mean age, patients with organic psychosis who reported delusions of jealousy tended to be younger than patients with organic psychosis without such delusions (Table 1) while patients with alcohol psychosis and delusions of jealousy tended to be older than those alcoholics without. However, these differences, along with the others, did not reach statistical significance.

Sex did seem to be of importance for the development of delusional jealousy (Table 1). With respect to all patients, delusions of jealousy were equally common in male and female patients, but in schizophrenia female patients were more likely to have delusions of jealousy ($P<0.01$), while in alcohol psychosis with delusional jealousy, male patients predominated ($P<0.01$).

Discussion

Delusions of jealousy have been described in different psychiatric disorders. The forensic aspects of this syndrome have been emphasised repeatedly (Gruhle, 1941; Lanzkron, 1961; Benezech *et al*, 1984). Podolsky (1961) identified jealousy as a motive in homicide; likewise Mowat (1966) and Shepherd (1961) both described jealousy as a "notoriously dangerous passion".

In our study, delusions of jealousy were most common in organic psychoses (7.0%), paranoid disorders (6.7%), alcohol psychoses (5.6%) and schizophrenia (2.5%), with the overall prevalence rate of all in-patients being 1.1%; thus delusions of jealousy are more than rare phenomena. The very low prevalence rate of 0.1% in affective disorders was a striking and unexpected result, which may be of differential diagnostic value in cases when classification in schizophrenia or affective disorder is difficult.

In paranoid syndromes, delusional jealousy usually occurs in its pure form as a monosymptomatic delusion. Crowe *et al* (1988) found that, compared with other paranoid patients with themes other than jealousy, individuals with jealous delusions were more likely to have a single delusion and a more benign course of the illness, yet the delusions tended to persist.

Besides paranoid disorders, delusions of jealousy could be found most often in organic and alcohol psychoses. In 1912 Schröder pointed out that "delusions of jealousy in alcoholics resemble similar conditions in senile and vascular dementia as well as in progressive paralysis". The comparatively frequent association of delusions of jealousy with alcoholism has gained specific psychiatric attraction. Whether it is still justified to see 'alcohol jealousy' as a diagnostic entity is a point of controversy. While in ICD-9 alcohol jealousy has its own classification among alcohol psychoses, DSM-III states that the "literature does not provide evidence to suggest the existence of the syndrome as an independent entity" (American Psychiatric Association, 1980). Alcohol jealousy in DSM-III can be expressed by diagnosis of a paranoid disorder in combination with alcohol dependence. As in paranoid disorders, alcohol jealousy usually takes a chronic course, although in some cases the delusions vanish if the alcohol abuse can be brought under control.

Musalek *et al* (1989) focused on the importance of sex and age for the development of different delusional themes and found that 69.2% of the patients with delusions of jealousy were male and that delusions of jealousy develop later in life than other delusions, for example those of persecution. On the other hand, Crowe *et al* (1988) reported a female:male sex ratio of 28:15 in jealous v. 28:30 in non-jealous patients. In alcoholics, delusional jealousy has been reported nearly exclusively in male patients (Soyka *et al*, 1989), while Vollmoeller (1983) pointed out that in schizophrenia delusions of jealousy prevail in female and younger patients. Our data suggest that age does not have a major influence on the development of delusional ideas in paranoid disorders, schizophrenia or alcohol psychosis, while sex seemed to be of some importance. In schizophrenia female clearly outnumbered male patients, while in alcohol psychosis delusions of jealousy could be found predominantly in male patients (sex ratio of 1:10). This might be explained by the higher prevalence rate of alcoholism in males, but the female:male ratio in alcohol psychosis *in toto* was only 1:2.5. A similar sex ratio for alcohol withdrawal delirium and alcohol hallucinosis has been reported before (Soyka *et al*, 1988, 1989; Soyka, 1989, 1990), probably reflecting the fact that 25–30% of all alcoholics are women.

In some cases it is difficult to decide whether ideas of infidelity are delusional or just 'obsessional'. In our study, few patients with personality disorder or neurosis were found to suffer from delusions of jealousy without other signs of psychotic symptoms. Delusions of jealousy in these disorders have been described before (Shepherd,1961) although diagnostic distinction from paranoid disorders, at least in cases with chronic delusions of jealousy, is very difficult. Catamnestic studies may show that a paranoid disorder emerges.

Delusions of jealousy occur either in pure form or as a major symptom of other psychoses. In most cases they become chronic. Characteristically, patients are convinced of the infidelity of the spouse without any proof. In many cases the spouse's 'partner' is unknown, and the patient often makes almost no effort to give evidence of the assumption. In other cases, the suspected partner is a colleague, close friend, or even relative, for example the son of one patient with organic psychosis. In delusional disorders independent from schizophrenia, delusions of jealousy predominate. Delusions of jealousy in schizophrenia are rarely isolated (Gruhle, 1940); the presence of sexual hallucinations are considered to be typical (Jaspers, 1910). For alcoholic jealousy, two forms have been differentiated (Soyka *et al*, 1989): a monosymptomatic 'Othello' type, without other delusions or hallucinatory symptoms, and a 'schizophrenia-like' type, with further delusions usually of persecution and verbal hallucinations. The second type probably has a very bad prognosis.

For the aetiology of delusional jealousy, various somatic, psychological and constitutional factors have been proposed. The development of delusional jealousy has been frequently associated with sexual disorders such as hypogonadism and impotence, which are frequent complications in different somatic disorders and in alcoholism (Llopis, 1962; Fahrner, 1987). Yet, in alcoholism, such sexual disorders are not a necessary condition for the development of delusional jealousy (Laux & Reimer, 1979); furthermore, alcohol-induced hypogonadism is often reversible (Castilla-Garcia *et al*, 1987) while delusions of jealousy usually persist. Shrestna *et al* (1985) could not find any clear correlations between the prevalence of sexual disorders and jealous ideas in alcoholics. Yet the fact that delusions of jealousy are common both in alcoholism and various organic psychoses supports the assumption of a 'somatic origin' of these delusions.

There is some literature on the psychology of delusional jealousy (Bechterew, 1989; Hahn, 1933; Fenichel, 1935; Retterstol, 1967; Tellenbach, 1967; Vauhkonen, 1968). Freud (1924) and later Fenichel (1935) and Lagache (1950) focused on the importance of latent forms of homosexuality for the development of the syndrome. Besides homosexual tendencies and abnormal sexual constellations (Retterstol, 1967), constitutional factors have been considered to play an important role in the development of delusions of jealousy.

The personality of patients with delusional thoughts has been described as sensitive, antisocial or paranoid (Scholz, 1930; Tiggelaar, 1956; Vauhkonen, 1968) with feelings of inadequacy or guilt due to thoughts of unfaithfulness being frequent. Cobb & Marrs (1979) concluded that jealousy is often associated with low self-esteem, lack of self-assertion, and sexual and marital problems. Docherty & Ellis (1976) proposed a typology of jealousy that consisted of excessive, obsessional-delusional and ego-dysfunctional forms. The psychological problems underlying delusions of jealousy have been discussed in depth by Enoch & Trethowan (1979).

Morbid as well as delusional jealousy is "notoriously difficult to treat" (Bishay *et al*, 1989). The therapy of delusions of jealousy depends on its diagnostic classification. Psychochemotherapy with neuroleptics may be of value and favourable results have been reported by Mooney (1965). Pimozide has proved to be efficient in some cases of delusional jealousy (Pollock, 1982; Munro, 1984).

Especially in schizophrenia, neuroleptics are the treatment of choice. With respect to chronic forms of delusional jealousy in alcoholics, the delusions vanish in some cases provided that alcohol abuse can be brought under control (Vauhkonen, 1968). Neuroleptics may be useful but in most cases the results are disappointing. As results of Crowe *et al* (1988) show, delusions of jealousy in paranoid disorders tend to be chronic, but have a better prognosis than non-jealous delusional disorders. For non-delusional forms of morbid jealousy, behavioural or cognitive psychotherapy may be of value (Cobb & Marrs, 1979; Bishay *et al*, 1989).

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Psychiatric Screening of Admissions to an Accident and Emergency Ward

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One hundred medical and surgical patients admitted to an accident and emergency ward were screened for psychiatric disorder. A psychiatric diagnosis was made in 37 patients, 32 of whom were correctly identified by the GHQ. Psychiatric morbidity was associated with being single, lower social class, unemployment, homelessness and living in Bloomsbury Health District or north-east London. It was also associated with not being registered with a GP. The 14 overdose patients were no more likely to receive a psychiatric diagnosis than other patients, yet constituted most of the psychiatric referrals. Few patients were asked by medical staff about emotional worries or problems. A desire to be asked such questions and a past psychiatric history were associated with a psychiatric diagnosis. Routine screening of psychiatric morbidity in both medical and surgical patients and appropriate psychiatric referral of identified patients is recommended. A system of facilitating GP registration is necessary, as much of the morbidity identified could be contained within primary care.

High levels of psychiatric morbidity in general medical in-patient populations have been identified in a number of studies (Maguire *et al*, 1970; Moffic & Paykel, 1975; Bridges & Goldberg, 1984; Feldman *et al*, 1987), yet medical staff still fail to detect the majority of psychiatric disorder (Mayou & Hawton, 1986). This study complements our study of attenders at an accident and emergency (A&E) department (Bell *et al*, 1990). It has the following aims: (a) to evaluate the prevalence and severity of psychiatric morbidity in patients newly admitted to an A&E ward, (b) to assess the association of socioeconomic factors with such morbidity, (c) to evaluate the extent of its non-detection, (d) to determine the usefulness of self-rated questionnaires as a means of detecting psychiatric morbidity in this setting, and (e) to assess the appropriateness of psychiatric referrals.

Method

The study was conducted on the A&E ward of University College Hospital (UCH) over 30 days, from early August to early September 1988. UCH is the main hospital for acute medical and surgical admissions in Bloomsbury, an inner-London health district of high socioeconomic deprivation (ninth highest in the UK and seventh highest in London according to the Jarman Under Privileged Area (UPA) score (Jarman, 1983, 1984)) with a large commuter population. Because of its location, UCH is frequently used by residents of adjacent health districts (notably Islington, and City and Hackney) and so those living in the North East Thames Regional Health Authority part of Greater London were considered separately from residents of other parts of Greater London.

The A&E ward admits all overdose and head-injury patients and, between 9 p.m. and 9 a.m., general medical and surgical admissions. All 144 patients aged 16–65 years admitted to the ward were included in the study. Basic sociodemographic data, details of registration with a general practitioner (GP) and presenting complaint were recorded for all 144 patients. One hundred (69.5%) patients agreed to complete the 60-item version of the General Health Questionnaire (GHQ-60; Goldberg, 1972, 1978) and the Hospital Anxiety and Depression Scale (HAD; Zigmond & Snaith, 1983), and to an interview using the Clinical Interview Schedule (CIS; Goldberg *et al*, 1970), the interviewer being blind to the GHQ and HAD scores. Reasons for exclusion included being unconscious (5), too ill (7), drunk (4), illiterate (3), inadequate command of English (14) or having no glasses when these were required for reading (4). Five refused and two were discharged before 8 a.m.

The CIS was originally developed to validate the GHQ and has been used in studies of psychiatric morbidity in general medical in-patient populations (Mayou & Hawton, 1986). Its limited coverage of psychopathology approximates to the greater proportion of psychiatric morbidity found in such populations, although we included additional questions to cover drug and alcohol problems. The CIS grading system of severity was as follows: 0, no disorder; 1, mild or transient disorder; 2, disorder requiring primary-care management; 3, disorder requiring psychiatric out-patient management; 4, disorder requiring psychiatric in-patient management.

Details of any past psychiatric history were obtained at interview. Patients were also asked if the medical team had asked them about psychiatric problems and whether they would have appreciated the opportunity to talk about such problems. Patients' notes were checked for details of mental state and a record was made of patients referred for psychiatric assessment.

The scores of medical in-patient populations on the GHQ have often been reported as higher than would be expected from community surveys (Goldberg, 1985). This finding

Table 1
Sociodemographic data

	Male no.	Male %	Female no.	Female %	Total %
Mean age: years	39.5		32.5		37.6
Marital status					
single	41	(56.2)	15	(55.6)	56
married	24	(32.9)	11	(40.7)	35
widowed	0	(0.0)	1	(3.7)	1
divorced	5	(6.8)	0	(0.0)	5
separated	3	(4.1)	0	(0.0)	3
Social class					
I	3	(4.1)	0	(0.0)	3
II	10	(13.7)	2	(7.4)	12
III	26	(35.6)	15	(55.6)	41
IV	21	(28.8)	4	(14.8)	25
V	13	(17.8)	6	(22.2)	19
Employment status					
employed	55	(75.3)	17	(63.0)	72
unemployed	18	(24.7)	10	(37.0)	28
Address					
no fixed abode	8	(11.0)	2	(7.4)	10
Bloomsbury	28	(38.4)	9	(33.3)	37
north-east London	13	(17.8)	7	(26.0)	20
other London	9	(12.3)	6	(22.2)	15
other UK	13	(17.8)	3	(11.1)	16
abroad	2	(2.7)	0	(0.0)	2
Ethnicity					
white British	65	(89.0)	23	(85.2)	88
white European	1	(1.4)	2	(7.4)	3
Afro-Caribbean	0	(0.0)	1	(3.7)	1
Asian	4	(5.4)	0	(0.0)	4
Far Eastern	1	(1.4)	0	(0.0)	1
Middle Eastern	0	(0.0)	1	(3.7)	1
North American	1	(1.4)	0	(0.0)	1
other	1	(1.4)	0	(0.0)	1
Total	73	(100)	27	(100)	100

Table 2
Psychiatric diagnoses and CIS severity rating

	Severity rating 2	3	4	Total No.	%
Depressive disorder	4	6	1	11	(29.8)
Manic–depressive disorder	0	0	1	1	(2.7)
Mixed anxiety/depressive disorder	7	3	0	10	(27.0)
Anxiety state/neurosis	9	0	0	9	(24.3)
Phobic anxiety disorder	0	1	0	1	(2.7)
Alcohol dependence syndrome	3	0	1	4	(10.8)
Narcotic addiction	1	0	0	1	(2.7)
Total	24	10	3	37	(100)

has been attributed to higher scoring on somatic symptoms. The threshold score for GHQ 'caseness' was therefore set at 13/14 after sensitivity and specificity analysis of the data showed this to be the most appropriate cut-off point. GHQ data are reported in this paper; HAD data will be reported separately. The appropriate pair-wise or between-group statistical tests of significance were selected for data analysis. Levels of significance were set at 0.05.

Results

Basic sociodemographic data of the 100 patients who participated in the study are given in Table 1. There were no statistically significant differences between this group and the 44 patients who did not complete the questionnaires, apart from ethnicity. Unemployment was higher in those under 26 years old ($\chi^2=6.77$, 1 d.f., $P<0.01$), was associated with being from social classes IV and V ($\chi^2=15.68$, 3 d.f., $P<0.005$) and homelessness or being resident in Bloomsbury or north-east London ($\chi^2=4.03$, 1 d.f., $P<0.05$). Interestingly, residents of Bloomsbury and north-east London had a similar social-class distribution to those from other parts of London and beyond ($\chi^2=0.56$, 3 d.f., $P<1.0$).

Thirty-two patients were not registered with a GP. This was associated with being younger (33.4 v. 39.4 years, Wilcoxon two-tailed test $P<0.05$) and single ($\chi^2=12.6$, 2 d.f., $P<0.05$) but not with sex, social class and address.

Sixty-two patients were admitted medically and 38 surgically. None of the above sociodemographic factors were associated with type of admission or with any particular presenting complaint.

A psychiatric diagnosis was made in 37 patients, of whom 32 were correctly identified as cases by the GHQ ($\chi^2=33.03$, 1 d.f., $P<0.0001$). The sensitivity of the GHQ was 86.5% and its specificity 73%. Positive predictive power of the GHQ was 65.5%. GHQ score correlated with severity rating (Kendall's tau$=0.452$, $P<0.0001$). Paradoxically, this correlation was higher in the 86 patients presenting with physical problems (tau$=0.469$, $P<0.0001$) than in the 14 patients admitted following overdoses (tau$=0.363$, $P<0.05$). The diagnostic categories and the severity rating of the disorders are shown in Table 2. A severity rating of 2 had been made in all five patients not identified as GHQ cases. Their diagnoses were anxiety state (3), alcohol dependence syndrome (1) and narcotic addiction (1). A subsidiary diagnosis of alcohol abuse was made in 13 patients (two being overdosed) and of personality disorder in eight patients (four being overdosed).

Twenty-five of the 37 patients (67.6%) who received a psychiatric diagnosis had a psychiatric history compared with only seven of the remaining 63 ($\chi^2=34.1$, 1 d.f., $P<0.0001$). Patients admitted following an overdose in whom a psychiatric diagnosis was made were no more likely to have a past psychiatric history ($\chi^2=1.3$, 1 d.f., Fisher's exact test $P<0.5$). Patients with a past psychiatric history were much more likely to be given a higher severity rating (Kolmogorov Smirnov$=0.658$, $P<0.0001$).

Twenty-six of the 37 patients (70.3%) who received a psychiatric diagnosis were single ($\chi^2=6.69$, 1 d.f.,

Table 3
GHQ 'caseness' and presenting complaint

	Cases		Non-cases		Total %
	no.	%	no.	%	
Cardiovascular	6	(12.2)	12	(23.5)	18
Gastrointestinal	10	(20.4)	4	(7.8)	14
Overdoses	10	(20.4)	4	(7.8)	14
Neurological	5	(10.2)	8	(15.7)	13
Head injury	7	(14.3)	5	(9.8)	12
Minor trauma	4	(8.2)	5	(9.8)	9
Genito-urinary/ gynaecological	1	(2.0)	7	(13.7)	8
Major trauma	0	(0.0)	3	(5.9)	3
Dermatological	2	(4.1)	1	(2.0)	3
Respiratory	1	(2.0)	1	(2.0)	2
Other	3	(6.2)	1	(2.0)	4
Total	49	(100)	51	(100)	100

$P<0.05$); patients from social class III were least likely to receive a psychiatric diagnosis ($\chi^2=16.62$, 3 d.f., $P<0.001$); patients of no fixed abode and residents of Bloomsbury and north-east London were more likely to receive a psychiatric diagnosis ($\chi^2=5.27$, 1 d.f., $P<0.03$) and to have a past psychiatric history (26 of 67 v. 6 of 33, $\chi^2=4.32$, 1 d.f., $P<0.05$). A psychiatric diagnosis was made in 18 of the 28 who were unemployed ($\chi^2=12.42$, 1 d.f., $P<0.0005$).

Patients not registered with a GP were more likely to receive a psychiatric diagnosis ($\chi^2=5.25$, 1 d.f., $P<0.05$), to be given a higher severity rating ($\chi^2=10.2$, 2 d.f., $P<0.01$) and to have a past psychiatric history ($\chi^2=20.1$, 1 d.f., $P<0.0001$). There was no association between any individual presenting complaint, including overdose, and GHQ 'caseness' (Table 3) and psychiatric diagnosis. Similarly, psychiatric diagnosis and severity rating were unrelated to whether the admission was medical or surgical.

Of the 14 patients admitted following overdoses, five reported not being asked about emotional problems by medical staff in the A&E ward. Twelve of the 14 patients were referred for psychiatric assessment. Of the remaining two, one was diagnosed as suffering from narcotic addiction (severity rating 2) and in the other, no diagnosis was made. Of the 12 referred, eight were GHQ cases but only six received a psychiatric diagnosis. The diagnoses were depressive disorder (2), mixed anxiety/depressive disorder (1), alcohol dependence syndrome (2), and manic-depressive disorder (1). In the remaining six patients, the overdose was in response to a relationship crisis.

Only seven of the 86 patients presenting with physical problems reported being asked by medical staff whether they had any emotional worries or problems, yet 44 said they thought it would have helped them to talk about important problems if they had been asked. The mean GHQ score of those who wished they had been asked was 25.7 compared with 8.1 for the remainder (Wilcoxon two-tailed test, $P<0.005$) and they were much more likely to receive a psychiatric diagnosis ($\chi^2=32.8$, 1 d.f., $P<0.0001$).

Comments relating to mental state appeared in the case notes of only seven patients. Severity of psychiatric disorder was unrelated to psychiatric referral ($\chi^2=4.6$, 3 d.f., $P<0.5$). Twelve of the 14 overdose patients were referred for psychiatric assessment, yet only four of the 29 patients presenting with somatic complaints and receiving a psychiatric diagnosis were so referred. Of these 29, 13 had a CIS severity score warranting psychiatric attention (3 or 4), while 16 had a score of 2, indicating the need for GP care.

Discussion

This is the first report of psychiatric morbidity in an A&E ward of both medical and surgical admissions. It is consistent with the findings of other studies of medical in-patients in identifying a high level of psychiatric morbidity (Maguire *et al*, 1970; Moffic & Paykel, 1975; Bridges & Goldberg, 1984; Feldman *et al*, 1987). It also demonstrates that the level of psychiatric morbidity in acute surgical patients differs little from that in medical patients. A subsidiary diagnosis of personality disorder was made in only 8% of patients. This was based on a clinical assessment and is almost certainly an underestimate (Malt *et al*, 1987).

The strong association demonstrated between psychiatric morbidity and a number of socio-demographic factors is in striking contrast to the findings of our study of attenders at an A&E department (Bell *et al*, 1990), but in keeping with a number of recent studies which have shown that socio-demographic characteristics of a population correlate not only with psychiatric morbidity but also with admission rates to psychiatric hospitals (Bluglass *et al*, 1980; Gibbons *et al*, 1983).

It has already been argued that indices of social deprivation such as Jarman's UPA score be used as a planning tool for estimating bed numbers and other resources for acute psychiatry (Hirsch, 1988; Royal College of Psychiatrists, 1989). The UPA score does not however include homelessness, a major social and health-care problem of inner cities, in its calculation of an area's level of social deprivation. Yet the scale of this problem is clearly reflected in this study, with 10% of patients having no fixed abode. Furthermore, these data raise the question of how to plan psychiatric liaison services to A&E in-patient units and indeed the liaison services in urban district general hospitals (DGHs) as a whole. To what extent should Jarman's UPA score and other indices of social deprivation be used in planning the liaison psychiatric needs of a DGH?

The majority of psychiatric morbidity went unrecorded (and therefore probably undetected) by medical staff who were no more likely to diagnose severe disorders than milder ones (Feldman *et al*, 1987). The strong association between patients saying that it would have helped to have been asked about emotional worries or difficulties and both GHQ 'caseness' and psychiatric diagnosis indicates that simple routine questioning by medical staff could be an efficient method of identifying psychiatric morbidity. As in our study of A&E attenders (Bell *et al*, 1990), asking about past psychiatric history, which has been shown to be a good indicator of prognosis (Hawton, 1981; Mayou *et al*, 1988), successfully identified 68% of cases, with few false positives. Nevertheless, the remaining cases were detected by the GHQ, which proved acceptable to patients and is a valid and reliable method of identifying psychiatric morbidity. Serious consideration should be given to its use as a routine screening instrument in all medical and surgical patients.

How can psychiatric resources be released to meet this hitherto undetected need? The pattern of referral identified – automatic referral of overdose patients and little else – while not unusual, is a cause for serious concern. It has been shown that adequate assessment of overdose patients can be carried out by nurses (Catalan *et al*, 1980) and social workers (Newton-Smith & Hirsch, 1979) provided they have adequate training and supervision. Implementation of such a policy would allow for psychiatric expertise to be directed more fruitfully towards the management of psychiatric morbidity detected by screening.

The large number of patients who were not registered with a GP and the association of this with psychiatric morbidity is in keeping with the findings of our study of A&E attenders (Bell *et al*, 1990). The study also demonstrates that non-registration is a problem which is not confined to inner-urban areas, although it seems likely that non-registered patients drift towards inner-urban A&E departments. This observation reinforces and extends our recommendation of facilitating GP registration. Ideally nationwide computerised information on general practices with vacancies on their lists could be displayed in all A&E wards and made available to non-registered in-patients.

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The Current Literature

Effect of Central Cholinergic Stimulation on Regional Cerebral Blood Flow in Alzheimer's Disease

KEN WILSON, DAVID BOWEN, PAUL FRANCIS and PHILIPPA TYRRELL

Patients with Alzheimer disease (AD) had reduced regional cerebral blood flow (rCBF) in the posterior parietotemporal region compared with controls, as determined with technetium-99m hexamethyl propyleneamine oxime and single photon emission tomography. Central cholinergic stimulation with physostigmine produced a focal increase in rCBF in the posterior parietotemporal region in the patients with AD but not in controls.

The summary quoted above is from an article by Geaney *et al* (1990). The present authors were invited to comment upon the study.

Ken Wilson

Geaney *et al* examined physostigmine-induced changes in regional cerebral blood flow (rCBF) in individuals with Alzheimer's disease and a normal control group. Eight subjects fulfilling DSM–III and NINCDS-ADRDA criteria underwent the Cambridge Disorders of the Elderly Examination (CAMDEX). All subjects underwent two single-photon emission computerised tomographic (SPECT) studies. Intravenous saline was administered in one and physostigmine in the other. A technetium-labelled agent (HMPAO) was used for imaging purposes.

The rCBF was quantified by finding the ratio between the activity in cerebral regions of interest and the cerebellum. Three slices were generated from each region of interest and the mean value was used in the calculation. The CAMCOG praxis score was used as an index of right-hemispheric function and the language score as an index of left-hemispheric function.

In those with Alzheimer's disease, rCBF was reduced bilaterally in the posterior parietotemporal regions and the administration of physostigmine increased the blood flow in the posterior left parietotemporal. The CAMCOG score correlated with rCBF in both posterior parietotemporal and anterior cortical regions of the Alzheimer sufferers. The neuropsychiatric cortical asymmetry correlated with the asymmetry of the cerebral blood flow.

Gustafsen *et al* (1987) studied the effects of an intravenous infusion of physostigmine on rCBF, electroencephalography (EEG) and cognitive performance in Alzheimer's disease. A xenon-133 inhalation technique was used to measure blood flow. Physostigmine infusion was associated with an increase in blood flow in the temporoparietal regions. Despite a comprehensive battery of cognitive tests, 'reaction time' was the only variable to respond to the physostigmine infusion when compared with the placebo. Smith *et al* (1986) suggested that the main effect of physostigmine on memory in normal volunteers was on attentional processes rather than mnemonic processes (storage and retrieval), which may explain this modest finding. Analysis of the EEG data demonstrated a diminished delta-wave power in the left hemisphere, which correlated with the physostigmine-induced increased blood flow.

Both these studies provide evidence for a diminished rCBF in the posterior parietotemporal regions of the brain and a physostigmine-induced improvement in the left hemisphere. Cognitive impairment has been correlated with the poor perfusion and improvement in EEG patterns and 'reaction-time' correlate with physostigmine infusions.

The authors draw attention to the potential use of SPECT in association with specific neurotransmitter challenge tests to obtain direct regional measures of transmitter function. This technique may well contribute towards neuroradiological and neurochemical diagnostic refinement, and the efficacy of SPECT in differentiating between multi-infarct dementia and Alzheimer's disease has been substantiated (Ebmeier *et al*, 1989). Future studies involving neurotransmitter challenge tests in the context of neuroradioimaging may provide a useful paradigm for differentiating between type I and II Alzheimer's disease. Initial SPECT studies demonstrate differences between groups determined by age of onset and duration of illness.

Burns *et al* (1989) examined 20 subjects meeting McCann's criterion and six controls using HMPAO as the agent for imaging. The patients were subdivided into those in whom amnesia predominated and those with concomitant aphasia and apraxia. The latter group had significantly reduced activity bilaterally in the temporal and posterior parietal lobes. Associations were found between the different cognitive functions and regions of reduced cortical perfusion. The age of onset and duration of the disease independently correlated with parietal and temporal activity.

Jagust *et al* (1990) examined the asymmetry of cortical blood flow in Alzheimer's disease found in previous studies in the context of pre-senile and late-onset Alzheimer subjects. All subjects fulfilled McCann's criterion. Neuropsychological testing included memory, verbal learning, delayed recognition, span tests, naming tests, word fluency and visuospatial tests. The pre-senile group were more severely demented than the late-onset group. For the entire group, disease duration and severity of dementia were significantly correlated, and the pre-senile subjects had a longer duration of illness than the late-onset subjects. There was a higher instance of apraxia in the pre-senile group. The parietal and temporal cortices showed lower perfusion than the frontal cortex in both groups. All regions in the pre-senile patients had significantly lower rCBF ratio, except for the right and left inferior frontal cortices: this results from the increased severity of illness in this group and is consistent with studies using positron emission tomography (PET) that have demonstrated correlations between severity of dementia and regional metabolism and perfusion. The SPECT perfusion imaging demonstrated a relative functional impairment of the left frontal cortex in the pre-senile group that was not found in the late-onset group and could not be explained by the more severe disease within this group. The authors were cautious in their interpretation of these results and drew attention to the asymmetrical left frontal involvement that is often found in patients suffering from late-onset Alzheimer's disease; such asymmetry is not a simple marker of early-onset disease.

The considered optimism expressed in Geaney *et al's* conclusion suggesting that SPECT challenge tests might provide a basis for the selection, development and monitoring of the effect of therapy for Alzheimer's disease patients may well have some justification. There are as yet unresolved issues that must be addressed before this can become a clinical reality. The neuroradiological classification of disease and in particular the heterogeneous nature of Alzheimer's disease must be refined before generalisations concerning the therapeutic effects of particular agents can be made. The changes in CBF associated with the infusion of such agents have to be correlated with sustained and measurable improvements in cognitive function that are of prognostic and therapeutic relevance before this technique will become widely accepted.

David Bowen and Paul Francis

Geaney *et al* have used rCBF as a marker of neuronal function in a disease where there appears to be a curious pattern of neuronal *degeneration*. It may be difficult to draw firm conclusions about the functional state, as the degenerative process probably produces cortical tissue deficient in neuronal subpopulations. The most straightforward intepretation of these blood-flow data is that in the parietotemporal region of the patients with Alzheimer's disease, many of the remaining neuronal structures are of a type that readily respond to acetylcholine. Control tissues, according to this hypothesis, would contain relatively more structures that do not readily respond to acetylcholine. This investigation may therefore define a pharmacological characteristic of neurones that are not particularly vulnerable to the process of Alzheimer's disease. Eventually, PET will probably provide the approach of choice for defining the characteristics of neurones that are selectively vulnerable. Such studies await the discovery of appropriate chemical markers.

The main chemico-anatomical problem in Alzheimer's disease appears to be degeneration of corticocortical glutamatergic pyramidal neurones in circumscribed areas of brain cortex (Bowen, 1990). The affected regions are the same as those identified by Geaney *et al*. Likewise, post-mortem brain sections from parietotemporal areas show more staining for neurofibrillary tangles than those from frontal and occipital regions (Esiri *et al*, 1990). Tangles, characteristically intracellular deposits in cortical pyramidal neurones, are not found to any significant extent in the neocortex of non-demented elderly brains (Perry, 1986). Moreover, they may be biochemically distinct (Spillantini *et al*, 1990) from the extracellular deposits of amyloid also seen in stained sections, typically as senile plaques. These can occur in appreciable numbers in brains of the elderly non-demented. In contrast to tangles, the amyloidosis is now under intensive study (Selkoe, 1990). Such work is possible as the cDNA sequence of amyloid precursor protein (APP) is known. However, it is not proven that the amyloidosis is other than a harmless by-product of the pathogenic mechanism. In contrast to plaques, the proteins comprising tangles are controversial, in particular the presence of proteins derived from APP (Caputo & Salama, 1989; Brion, 1990). It is, therefore, not widely accepted that extracellular amyloidosis 'drives' tangle formation.

Amyloid formation appears to be due to abnormal cleavage of a normal cell surface protein (APP) since the normal cleavage site seems to lie within the region

(A4 or beta-protein domain) of the APP molecule that is deposited as senile plaque amyloid. The most straightforward possibilities (Glenner & Melhaff, 1990), are that amyloidosis is caused by either inhibition of proteolytic cleavage of the A4 domain or by enzyme induction of methionyl-aspartyl proteolysis (residues 596 and 597 of APP; residue 597 is the N-terminus of A4 protein). Clearly, if this proteolytic cleavage in an Alzheimer's patient can be inhibited, the amyloidosis should be prevented.

The excitement of the work on APP has overshadowed the tangle and pyramidal neurone, yet despite the intensive research, the central issue of the curious pattern of degeneration is unexplained in terms of the amyloidosis associated with either formation of senile plaques or the meningeal and cerebral blood vessels (Selkoe, 1990). Opinion is divided as to whether the study of amyloidosis in Alzheimer's disease is a rational route towards developing specific therapies for this still untreatable disease (Caputo & Salama, 1989; Selkoe, 1990).

Our approach has been to study events associated with corticocortical glutamatergic neurones. Previously, cerebrovascular degeneration had been highlighted in the brains of the demented. It was the seminal study of Corsellis (1962), on the distribution of brain pathology in many consecutive post-mortem examinations at Runwell Hospital, that helped to lay emphasis on plaques and tangles. In addition to these lesions, Alois Alzheimer found in the index brain that 'numerous ganglion [pyramidal] cells, particularly in the upper cell layers, had disappeared entirely' (see Bowen, 1981). The biochemical and pharmacological properties of these cells are not well understood, but this should improve as methods are under development for destroying them selectively in laboratory animals (Crino *et al*, 1990; Pangalos *et al*, 1990). Moreover, there is the basis of a treatment strategy aimed at the corticocortical neurone using a low dose of the antituberculous drug D-cycloserine, a partial agonist at the N-methyl-D-aspartate receptor complex (Monahan *et al*, 1989; Bowen, 1990; Procter *et al*, 1990; Watson *et al*, 1990).

Philippa Tyrrell

This paper convincingly demonstrates an increase in rCBF in the posterior parietotemporal regions of patients with dementia of the Alzheimer type (DAT) following an intravenous dose of physostigmine, which was not observed in normal subjects. This observation has implications for our understanding of regional neurotransmitter changes in degenerative dementias, and raises important questions about the role of cholinergic replacement therapy.

Using $^{15}O_2$, PET studies can obtain absolute quantitative measurements of rCBF, as compared with the relative quantification of SPECT studies, which are expressed as ratios of tissue of interest to cerebellar values. In addition $^{15}O_2$ studies also provide absolute measurements of regional cerebral oxygen metabolism ($rCMRO_2$), together with regional oxygen extraction ratio (rOER). Alternatively, ^{18}FDG (^{18}F-fluorodeoxyglucose, a glucose analogue) can be used to measure absolute values of fluorodeoxyglucose metabolism. PET studies have shown that rCBF is matched to $rCMRO_2$ in normal states and in degenerative and vascular dementias (Frackowiak *et al*, 1981), because the reduced cerebral oxygen supply is appropriate for the diminished metabolic demands of damaged tissue. As a result, measurement of rCBF with SPECT provides similar patterns of hypometabolism to those observed with PET; this has been confirmed in a number of SPECT studies (e.g. Burns *et al*, 1989). The advantage of using SPECT is that it is a more easily available technique, but the quantification is relative rather than absolute, and only rCBF can be measured.

One problem with pharmacological rCBF challenge studies is that a drug may increase blood flow without altering cerebral metabolism, because the increase in rCBF is accompanied by a reduction in the rOER. One PET study of patients with multi-infarct dementia treated with a vasodilator agent showed a transient rise of rCBF in 6 of 14 patients studied; this increase in flow was associated with a reciprocal fall in rOER, so that the $rCMRO_2$ remained constant (Gibbs *et al*, 1986). The change in rCBF was therefore physiologically irrelevant. This is a possible criticism of another study in which an increase in rCBF in response to the cholinergic agent L-acetyl-carnitine was observed (Battistin *et al*, 1989). However, this study, in contrast to the present study, included no control subjects. It would seem unlikely that acute administration of physostigmine would increase rCBF alone in demented subjects but not in normals, but it would be interesting to try to repeat the observation using $^{15}O_2$ and PET to ensure that it is indeed an increase in cerebral metabolism that is being measured.

A characteristic pattern of change of rCBF, as measured with SPECT or PET, is observed in many patients with DAT. The pattern is not diagnostic, however, as similar changes are observed, for example, in Creutzfeldt–Jakob disease (Friedland *et al*, 1984). The posterior temporal and parietal areas are most affected, usually bilaterally (Frackowiak *et al*, 1981), but asymmetry is observed in some patients; for example, those with prominent speech abnormalities have a predominant left-sided deficit.

The distribution of the rCBF/rCMRO$_2$ deficit is similar to the distribution of maximal histopathological change and also to the distribution of maximal cholinergic abnormality (measured by the activity of the marker enzyme choline acetyltransferase, ChAT) (Procter *et al*, 1988). The exact relationship between metabolic activity, neuronal loss, and loss of cholinergic nerve terminals is a matter for speculation, but there is a correlation between the severity of dementia and the number of neurofibrillary tangles, the severity of the ChAT deficit (Wilcock *et al*, 1982), and the degree of hypometabolism on PET scan (Frackowiak *et al*, 1981).

Since the discovery of the ChAT deficit in 1976, there has been considerable interest in the use of cholinergic agonists as a treatment of the symptoms of the DAT. Scopolamine, an anticholinergic agent, has been shown to cause impairment of memory storage and retrieval in normal subjects, but physostigmine administration resulted in no alteration of memory or other cognitive functions (Drachman & Leavitt, 1974). Enhancement of the cholinergic system in DAT patients has been attempted using choline and lecithin (a choline-containing phospholipid) without improvement in double-blind trials (Thal *et al*, 1981). Administration of physostigmine, by contrast, in eight patients with early DAT increased total recall and retrieval from long-term storage in six of the patients, related to the degree of cholinesterase inhibition in the cerebrospinal fluid, suggesting that the degree of improvement was related to the amount of physostigmine that reached the brain (Thal *et al*, 1983). Physostigmine is a cholinesterase inhibitor, so presumably it acts by maintaining whatever acetylcholine is present in the synaptic cleft. It would seem likely that the drug would be most effective in patients with relatively intact cholinergic systems, that is, patients with relatively mild dementia. However, a recent study of 22 patients treated with oral physostigmine showed no greater benefit in patients with mild rather than moderate dementia (Stern *et al*, 1987). In addition, in this study physostigmine administration improved performance on tests of attention and visuospatial ability, rather than memory.

Geaney *et al* have not documented any changes in cognitive performance before and after administration of physostigmine to correlate with the observed changes in rCBF, although this is presumably work in progress. The results of clinical trials with this drug are not clear cut, and some patients may respond while others do not. Large numbers of patients may be required before any clear correlation between increase in rCBF and improvement in cognitive performance is obtained. It would be of interest to compare changes in rCBF in 'responders' and 'non-responders' to the drug, and to compare different clinical subgroups of DAT (for example, mild and severe dementia, and patients with predominantly left- or right-hemisphere abnormalities).

This study raises many interesting questions and is likely to be the forerunner of a number of studies which may offer some insight into the effect of pharmacological manipulation on cognitive function and rCBF.

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Point of View

The Functional Psychoses – Are Oncogenes Involved in Their Pathogenesis? Some Speculations

JOHN LEACH

Oncogenes are genes whose expression has been associated with malignant transformation of cells in tissue culture and with neoplastic change *in vivo* (Bishop, 1987). Much of the current understanding of their nature and action has stemmed from work, over the past 20 years, on tumour viruses (Temin, 1971; Rapp, 1983). One group of tumour viruses, the retroviruses, are unique in possessing an enzyme, reverse transcriptase, which transcribes to the cell DNA a copy of the viral RNA genome (Marks, 1987). After the discovery of viral oncogenes, such DNA copies were used as probes in hybridisation studies (Stehelin *et al*, 1976; Frankel & Fischinger, 1976). These probes, capable of annealing to complementary DNA sequences, revealed the existence of the latter in normal, unaffected cells (Willecke & Schäfer, 1984). These sequences, called cellular or proto-oncogenes, exist in a wide range of eukaryotic organisms, from yeast to man.

The main thrust of oncogene research has been concerned with elucidating mechanisms of neoplastic change with a view to improving the prophylaxis and treatment of cancer. In respect of the central nervous system, this work has resulted in an increased understanding of the pathogenesis of some neural tumours (Breakefield & Stern, 1986; Fujimoto *et al*, 1988) and an appreciation that oncogenes can be expressed in normal neural tissue (Hunt *et al*, 1987). Its relevance for psychiatric illness, if any, has hardly been considered (the exception, the work of Crow, is outlined below), although a related field, a postulated viral role in the aetiology of the functional psychoses, has stimulated a great deal of research.

Background

The first suggestion of a link between viruses and the functional psychoses is attributed to Menninger. In the aftermath of the 1918 influenza epidemic, he noted similarities between the psychiatric symptoms of some post-influenzal individuals and those of patients with schizophrenia and affective disorder (Menninger, 1926, 1928). Interest in this area was rekindled, during the following three decades, by papers noting a temporal relationship between viral infection and the onset of psychosis in some patients (McCowan & Cook, 1928; Goodall, 1932; Weinstein *et al*, 1955).

There is a substantial body of research examining a postulated role of viruses in psychosis. Viral involvement in schizophrenia and affective psychosis has been investigated by estimating titres of viral antibodies in sera and cerebrospinal fluid of patients (e.g. Lycke *et al*, 1974; Albrecht *et al*, 1980; King *et al*, 1985) and by assessing immune function (Cappel *et al*, 1978; DeLisi *et al*, 1982; Coffey *et al*, 1983). Results have been inconsistent and are, in any case, difficult to interpret in isolation (King & Cooper, 1989). In addition, the role of viruses in schizophrenia has been examined using cell culture techniques (Crow *et al*, 1979; Tyrrell *et al*, 1979) and transmission experiments (Baker *et al*, 1983). This work has not, to date, provided strong evidence for a viral role.

While viruses have stimulated psychiatric research, oncogenes have, in the main, been ignored by psychiatrists. The work of Crow is exceptional in this respect. During the 1980s, he has developed a number of linked hypotheses concerning a 'virogene', a viral sequence of bases incorporated into the human genome (Crow, 1983, 1984, 1986*a*, *b*, 1987, 1988). Virogene expression is held to produce psychosis. In respect of schizophrenia, Crow's theory incorporates findings of structural asymmetry in the brains of some patients (Crow, 1988) by hypothesising that the virogene interacts with a cellular oncogene. The latter, presumably through control of a growth factor, is responsible for hemispheric asymmetry and cerebral dominance. The virogene, which could result from a retrovirus, is acquired by perinatal infection or in the germ line from an infected parent.

This highly original theory emphasises the role of oncogenes in growth and development. This, because of concern with tumorigenesis, is their most researched role. However, their involvement in cellular function is much wider. Work during the past decade indicates that oncogenes are able to modulate some of the most basic physiological processes of the cell. Many of these processes assume particular interest for psychiatry. This can be inferred from reports that some are abnormal in groups of psychotic patients. It is emphasised by the fact that treatments of known but ill-understood therapeutic value in psychosis are known to interact with oncogene-mediated systems.

Mechanisms of pathogenesis?

Despite a large and increasing volume of research, the effects of oncogenes on cellular function remain little understood. Certain important facts are known, however, and these have provided a scaffolding around which hypotheses of oncogene function have been constructed. Three related areas are of particular interest here. They concern the interaction of oncogenes with:

(a) receptors, neuropeptides and neurotransmitters
(b) cellular second-messenger systems
(c) calcium metabolism.

(a) Receptors, neuropeptides and neurotransmitters

A number of findings suggest that oncogenes might be involved in neurotransmitter function. It has been shown (Matrisian *et al*, 1988) that oncogene-transformed fibroblasts express RNA for prepro-enkephalin, one of the precursors to a family of encephalin peptides that are active in the brain. This process is specific to certain types of oncogenes and cells, suggesting the activation of a specific oncogene-linked cellular signalling system (see (b) below). By implication, such an oncogene, via a particular neuropeptide, might modulate a specific neurotransmitter. Encephalin, for example, is known to occur in noradrenergic and serotoninergic neurones (Mackay, 1985).

Modulation of neurotransmitters could also occur through alterations in receptors. The mas oncogene has been shown to encode an angiotensin receptor with mitogenic activity (Jackson *et al*, 1988). (Oncogenes are named by a three-letter code derived from their associated neoplastic disease, sometimes with prefixes v and c to designate viral or cellular, while other prefixes, as in H-ras, K-ras, distinguish oncogene subtypes.) Such mitogenic activity occurs *in vivo*, not *in vitro*, presumably resulting from stimulation by the receptor ligand, an angiotensin. The mitogenic properties of this receptor suggest that

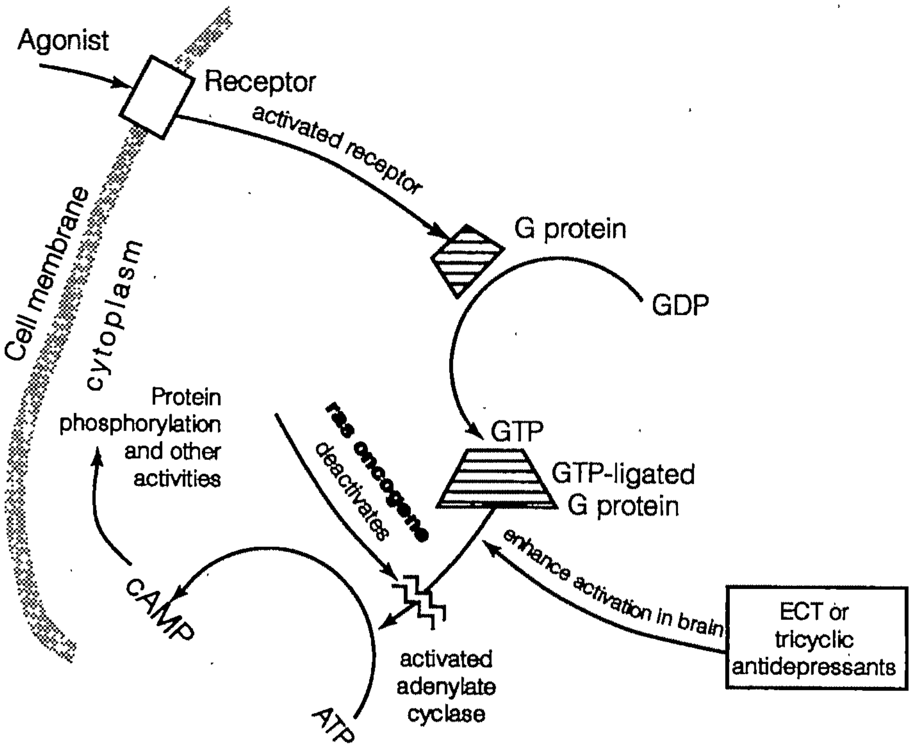
Agonist
Receptor
activated receptor
G protein
GDP
GTP
GTP-ligated G protein
Cell membrane
cytoplasm
Protein phosphorylation and other activities
ras oncogene deactivates
enhance activation in brain
ECT or tricyclic antidepressants
cAMP
ATP
activated adenylate cyclase

Fig. 1 Highly simplified representation of the cyclic AMP second-messenger system (AMP, adenosine monophosphate; ATP, adenosine triphosphate; GDP, guanosine diphosphate; GTP, guanosine triphosphate; G, guanine nucleotide-dependent coupling protein).

some neural peptides function as growth factors and may be important in the development of the nervous system. The link with Crow's work is clear.

(b) Cellular second-messenger systems

Neurotransmitters exert their effect via receptors. These in turn are linked, within the cell, to so-called second-messenger systems, which function as signal amplification and effector mechanisms. Two such systems, employing cyclic adenosine monophosphate (AMP) (Limbird, 1981; Michell, 1989) and inositol lipids (Michell, 1979; Berridge, 1986), have been extensively researched. There are data linking both with affective psychosis. Both interact with oncogenes.

In the cyclic AMP system (Fig. 1), cyclic AMP is activated by the enzyme adenylate cyclase. The activation of adenylate cyclase involves a complex interaction between the hormone receptor (e.g. the beta-adrenergic receptor) and a so-called G (guanine nucleotide-dependent) coupling protein. The cyclic AMP formed facilitates important cellular processes (e.g. the activation of protein kinases) (Stryer, 1981).

The second system, the inositol lipid pathway (Fig. 2), has been the subject of considerable interest in recent years as its biochemistry and potential significance have become better understood. The key event in this pathway is the hydrolysis of an inositol lipid, phosphatidylinositol 4,5-bisphosphate (PtdIns(4,5)P_2). This generates two substances, diacylglycerol and inositol triphosphate. Inositol triphosphate, in the cytoplasm, mobilises intracellular calcium (Lopez-Rivas & Rozengurt, 1983).

In rats, the cyclic AMP second-messenger system in brain has been shown to be affected by long-term administration (15–20 days) of tricyclic antidepressives or electroconvulsive therapy (ECT) (Menkes *et al*, 1983). This is associated with an increased activation of adenylate cyclase (Fig. 1). Further work indicated that this activation resulted from an enhanced interaction between a protein and adenylate cyclase.

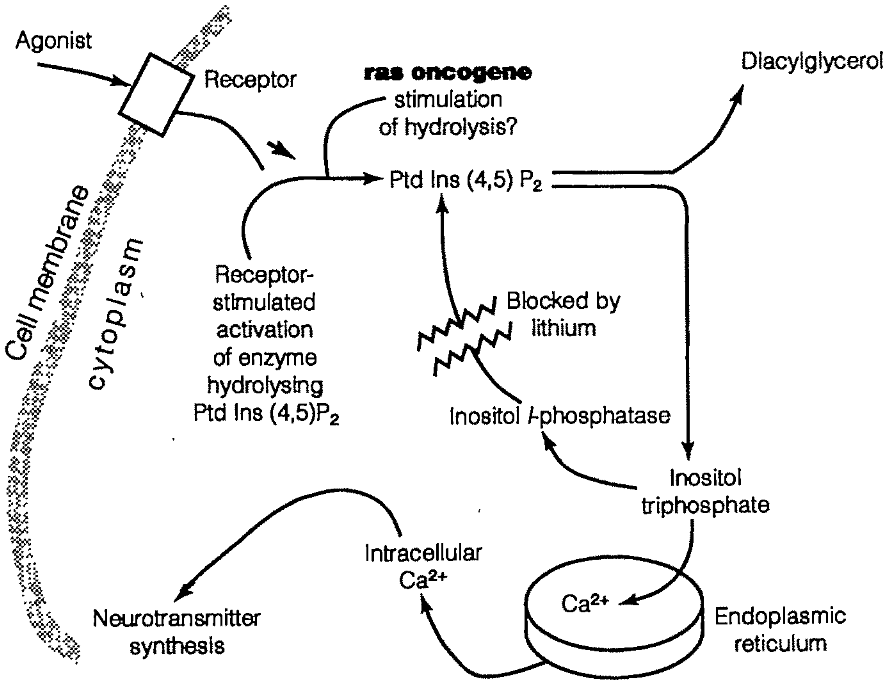

Fig. 2 Highly simplified representation of the inositol lipid second-messenger system (PtdIns(4,5)P_2, phosphatidylinositol 4,5-bisphosphate).

Ras oncogenes code for G proteins (Levinson, 1986). They produce 21 kDa-proteins (p21s) with intrinsic guanosine triphosphatase (GTPase) activity. The human bladder ras oncogene, EJ/T24, is activated by a point mutation at codon 12. Murine fibroblasts, transformed by EJ/T24, show a deactivation of adenylate cyclase (Chiarugi *et al*, 1985).

Chiarugi *et al*, in the work noted above, found that ras-transformed fibroblasts also showed changes in the inositol lipid second-messenger system. In contrast to the deactivation of adenylate cyclase, ras transformation stimulated hydrolysis of inositol lipids. It is possible that the mutated ras gene causes an uncontrolled stimulation of PtdIns(4,5)P_2 phosphodiesterase, the enzyme that hydrolyses PtdIns(4,5)P_2 (Fig. 2). This may occur because the point mutation at codon 12 abolishes the GTPase activity of p21. In its absence the system is unable to switch off and the products of PtdIns(4,5)P_2 hydrolysis, diacylglycerol and inositol triphosphate, are generated *ad infinitum* (Berridge, 1986).

Lithium, used most extensively in the prophylaxis and treatment of manic–depressive psychosis, inhibits an enzyme, inositol l-phosphatase, which facilitates the regeneration of PtdIns(4,5)P_2 (Wood & Goodwin, 1987). It thus blocks the process initiated by oncogene activation. One interpretation of these data is that the inositol lipids depleted by lithium are linked to a neurotransmitter system or systems whose activation is involved in the onset of manic illness. This would explain lithium's prophylactic effect. It would follow from this that oncogene activation, by stimulating uncontrolled production of inositol lipid, could precipitate manic illness. It might be significant, in this context, that an important function of the pathway potently inhibited by lithium is the mobilisation of intracellular calcium (Joseph *et al*, 1984).

(c) Calcium metabolism

The level of intracellular calcium controls neurotransmitter synthesis (Rubin, 1970; Phillis, 1974; Bunney & Murphy, 1976). Two main mechanisms determine levels of intracellular calcium. One is its release from intracellular storage sites in endoplasmic reticulum. This, as noted in (b), is one function of the inositol lipid pathway (Fig. 2). The second is control of plasma membrane permeability to calcium via the regulation of specific calcium channels (Miller, 1987).

An involvement of calcium in psychotic illness is suggested by reports of psychotic patients successfully treated with calcium-channel blockers. Such drugs have proved effective in some patients with mania (Dubovsky *et al*, 1982) and have caused depression (Hullett *et al*, 1988). Phenothiazines, therapeutic in mania, antagonise the action of intracellular calcium by binding to calmodulin (Antman *et al*, 1980). Furthermore, recurrent acute onsets of mania and psychotic agitation have been shown to be associated with transient increases in serum calcium and phosphorus (Carman *et al*, 1979).

Oncogenes closely interact with the mechanisms regulating the concentration of intracellular calcium. It has been noted that activation of the ras oncogene, via the inositol lipid pathway, stimulates release of intracellular calcium. It is now known, in muscle at least, that oncogene activation can also block the induction of both calcium and sodium channels (Caffrey *et al*, 1987). Oncogenes, therefore, seem capable of wide-ranging modulation of the calcium concentration of cells, which implies that their effects on neurotransmitter function are equally extensive.

Investigation

Investigation of a putative role of oncogenes in the pathogenesis of the functional psychoses could utilise two complementary research strategies: the first, employing restriction fragment length polymorphisms (McGuffin, 1988; Mullan & Murray, 1989), would involve a search for linkage in patients' families using the chromosomal location of cellular oncogenes as 'candidate regions'; the second, if linkage is established, would attempt to identify the nature of the link between oncogenes and psychosis.

In respect of the first strategy, no positive linkage has yet been established between psychosis and oncogenes. A finding of linkage between bipolar affective psychosis and the c-H-ras 1 oncogene in an Old-Order Amish pedigree (Egeland *et al*, 1987) was not replicated in Icelandic, American and Irish pedigrees (Hodgkinson *et al*, 1987; Detera-Wadleigh *et al*, 1987; Gill *et al*, 1988) and has recently been withdrawn (Kelsoe *et al*, 1989). This, in itself, does not invalidate the hypothesis that a link between oncogenes and psychosis exists. With at least 46 oncogenes distributed non-randomly throughout the human genome (Hecht, 1988), the hypothesis can only adequately be tested by a series of linkage studies. Moreover, the situation is complicated by the fact that heterogeneity of expression is characteristic of oncogenes. It is known, in relation to tumorigenesis, that the same oncogene, activated in different tissues, can give rise to different tumours in each. Conversely, the same tumour may be associated with the activation of different oncogenes (Emery, 1984; Marks, 1987). This suggests that some bipolar pedigrees, for example, while not showing linkage with c-H-ras, might do so with other oncogenes.

The second research strategy could employ a variety of techniques. Cloned DNA oncogene sequences could be used to search for mutations in the homologous sequences of patients (Gurling, 1988). Clarifying gene structure would elucidate pathogenesis, as occurred, for example, with the thalassaemias (Emery, 1984). More specifically, recent work has shown that mapping of epitopes within the ras p21 molecule recognised by monoclonal antibodies has made it possible to recognise important functional regions within that molecule (Lacal & Aaronson, 1986). Such work illustrates one aspect of what will, of necessity, be a multifaceted inquiry. The links between oncogenes and neurotransmitters (or other agents of psychosis) are likely to be complicated and regulated by many intermediaries.

In conclusion, it is perhaps most important to state explicitly that there is no evidence confirming a link between oncogene activity and the functional psychoses. Having said that, the known activities of oncogenes impinge, in many ways, upon biological processes thought to be important in the pathogenesis of these illnesses. This interaction is potentially significant and merits investigation. Interestingly, the case for oncogene involvement in pathogenesis is stronger in affective psychosis. A link between oncogenes and schizophrenia is less apparent. This might be a valid conclusion or reflect relative ignorance of the processes involved.

The hypothesis that oncogene activation contributes, in a substantial way, to psychosis, raises many questions. What causes this activation? Why does it occur in some members of genetically susceptible families and not others? How can it be reconciled with the periodic or cyclical onset of symptoms in some patients? These questions are, at present, unanswerable. They do not, by that fact, disprove the hypothesis.

Detailing different oncogene activities as seemingly discrete phenomena has the value of focusing attention. It is, however, misleading in its simplicity and it will be apparent that the different oncogenic processes interact to a greater or lesser extent. It is equally apparent, as daily new facts about oncogenes emerge, that we are very far from seeing the whole. Oncogene interaction with hormones (Bishop, 1986; Smith *et al*, 1986), and other genes (Jones, 1986; Jaggi *et al*, 1988) are just two areas that seem likely to impinge upon psychiatry in the coming years. There may be many more.

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British Journal of Psychiatry (1991), **158**, 569–578

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Editor: Ian Pullen

Contents: Vasopressin in polydipsia/Psychotic depression presenting as status epilepticus/Recording of information in case notes/Motor disorders of the mentally handicapped/Engagement of relatives in intervention programmes/Patient data in child psychiatry/Child psychiatry liaison services/Beyond pumpkin seeds/Blinding trials/Demand for psychogeriatric services/How old are the elderly?/The 'new cross-cultural psychiatry'/Informed consent in India/Clozapine-treated NMS/All-night television can damage your health/Toluene-related psychosis.

Vasopressin in polydipsia

Sir: Delva *et al*, in their paper on vasopressin (AVP) secretion and action in polydipsic chronic psychiatric patients (*Journal*, November 1990, **157**, 703–712), are unable to reproduce our findings that these patients (a) maintain the normal linear relationship between plasma vasopressin and plasma osmolality but exhibit a lower set point for vasopressin release, and (b) exhibit an apparently enhanced renal sensitivity to AVP's action (Goldman *et al*, 1988). Instead they find (a) no correlation between these patients' inappropriately elevated plasma AVP and concurrent plasma osmolality (Type I syndrome of inappropriate antidiuretic hormone (SIADH)) and (b) a normal to depressed renal sensitivity to AVP. While the authors allude to differences in method between the two studies, I believe they do not appreciate how these differences limit the ability to interpret their data.

The authors determine the relationship between plasma vasopressin and plasma osmolality by measuring these variables over several days in a naturalistic design; patients drank freely, moved freely, and smoked freely except for the hour prior to blood drawing. They compared these results with those obtained in normals using the standard controlled assessment of vasopressin secretion (oral water load (usually 20 cc/kg)) followed by urine collection every 30 minutes for four to five hours, and/or a two-hour regulated infusion of hypertonic saline (patient is kept supine, while smoking and food intake is carefully restricted). The authors do not point out that data collected by these two disparate methods may not be (and in my opinion are not) comparable. Specifically, neither the authors nor others have provided data showing that normals studied in a similar 'naturalistic' manner still exhibit a linear correlation between plasma vasopressin and plasma osmolality. Furthermore, recent data show that the effects of smoking on vasopressin function are apparent for at least 90 minutes (Allon *et al*, 1990), suggesting Delva *et al*'s 60-minute smoking restriction is inadequate.

The authors use data obtained using the same basic design to assess renal sensitivity to AVP's actions. Besides the previously mentioned limitations, the authors utilised our data to define this range of normal, although we use different assays, and thus would be expected to generate different ranges. I believe their results are uninterpretable unless they define the normal range with their own assay using their design (pooled four-hour urines). I also believe pooling samples for four hours significantly reduces the sensitivity of this measure.

Finally, the authors suggest that the apparent renal hypersensitivity to AVP in our patients was due to polydipsia-induced incomplete bladder emptying. While we cannot exclude this possibility (although we have no proof of bladder dysfunction in any of the subjects), Emsley *et al* (1989) reported findings similar to ours using the standard controlled assessment in drug-free non-polydipsic schizophrenics. Hence other factors, currently unknown, are more likely to account for this finding.

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Authors' Reply: In response to the letter from Dr Goldman, we should point out that our study demonstrated heterogeneity among polydipsic chronic psychiatric patients for the presence and subtype of SIADH. Of the twelve patients, three demonstrated no abnormality, seven demonstrated Type I SIADH and two demonstrated Type II SIADH. We explicitly stated that the differences between the findings of Goldman *et al* (1988) and our own might have resulted from a number of differences in experimental design, or from patient heterogeneity.

We believe that our assessment of the relationship between plasma AVP and serum osmolality is valid because the control group was assessed with the same assay under similar conditions. The control subjects were sitting where the blood was taken and the period of half an hour of sitting was chosen purposely to accommodate the fact that plasma AVP reaches a basal level by this time. There is no reason to suspect that normals studied in a similar 'naturalistic' design would not continue to exhibit a linear correlation between plasma vasopressin and plasma osmolality. Your correspondent notes that Allon *et al* (1990) have investigated the effects of smoking on renal concentrating ability, but the relevance of this study to Goldman's critique is doubtful as, in the Allon study, no measures of vasopressin were made. Our article reviewed the literature on the effects of smoking on vasopressin levels and we are not persuaded that smoking was the cause of the inappropriately high vasopressin levels in our patients.

Regarding the assessment of renal concentrating ability, we think that the similarity of the normal ranges of plasma AVP versus plasma osmolality in the two studies, both of which used radio-immunoassays for the measurement of AVP, justifies the use of the normal range of plasma AVP versus urine osmolality provided by Goldman *et al*. We agree that the pooling of urine over four-hour periods does somewhat reduce the precision of the estimates of urine osmolality, but the main subject of our investigation was vasopressin secretion rather than urine concentrating ability and our findings regarding the latter are consistent with decreased renal concentrating ability seen in normal subjects on prolonged high fluid intake. As we have mentioned, bladder dysfunction is common in these patients, and as a result an ideal method for the study of urine concentrating ability would have to employ bladder catheterisation. Unless this is done, any data concerning renal function must be interpreted with caution.

Emsley *et al* (1989) found that untreated psychotic patients without polydipsia dilute their urine less efficiently than normals after fluid loading; some patients had higher than normal baseline levels of vasopressin, and these patients showed the most pronounced antidiuretic states. The fact that non-polydipsic, recently admitted, untreated psychotic patients have these abnormalities is not surprising. Whether chronically polydipsic pyschotic patients have an abnormality in urinary diluting capacity independent of abnormally high plasma levels of AVP remains moot.

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Psychotic depression presenting as status epilepticus

Sir: Griffiths & Farmer (*Journal*, December 1990, **157**, 909–911) reported a case of status epilepticus secondary to water intoxication, which in turn was secondary to a depressive psychosis. The patient admitted brief episodes of low mood over the previous ten years associated with an increase in fluid intake.

We were very interested to read this report since, as the authors state, there is a paucity of literature on water intoxication in subjects other than chronic schizophrenic patients. However, another perspective can be provided by a recent paper (Allon *et al*, 1990) reporting investigations of two schizophrenic patients admitted with hyponatremic seizures, and suggesting that cigarette use may contribute to the development of hyponatremia by impairing water excretion.

In their paper, Griffith & Farmer did not mention whether the patient was a smoker, and reported that renal response to water loading was not assessed. It would be interesting to know whether the patient was a smoker, and if that was the case, if her consumption was greater during the depressive episodes. The higher prevalence of heavy smoking in chronic schizophrenic patients than in ambulatory depressive patients could perhaps explain the fact that water intoxication occurs predominantly in the former category.

The common point between schizophrenics and depressives, concerning tobacco, is perhaps the fact that they use it as an escape from boredom and as a stimulant.

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Recording of information in case notes

SIR: The medical defence societies regularly draw the attention of consultants to the proper recording of information in case notes, as it can have both clinical and medico-legal consequences. The fact that inadequacies continue, even in this increasingly litigious age, is regularly brought home to one of us (DD), in the capacity of second opinion appointed doctor and Mental Health Commissioner.

An audit of the use of lithium carbonate was conducted (by PLC) in a small district general hospital psychiatric unit. Of 73 patients on lithium treatment the case notes of 25 were randomly selected and studied in detail to investigate the adequacy of record-keeping and monitoring of treatment. In only two case notes was there any mention of information given about lithium treatment before it was started, and in no case notes was there any mention that the patient had been informed of the adverse and toxic effects, the need for monitoring, the need to maintain adequate fluid intake and so on.

It seems likely that if a similar survey was performed in most hospitals in this country, the same results would be obtained. Lithium is known to be a toxic drug, and patients are almost certainly counselled about its use, but there should be some mention of this in the case notes. If we fail to make notes in the case of such potentially dangerous drugs, we are much less likely to do so when the drug profile causes us less anxiety. If this was a routine practice some colleagues would have been able to avoid the heartache caused by the impending litigation over benzodiazepine dependence, where one of the most frequent allegations being made is that inadequate information was given about dependence and the need for gradual withdrawal.

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Motor disorders of the mentally handicapped

SIR: We agree with Rogers *et al* (*Journal*, January 1991, **158**, 97–102) that a crucial point in the motor disorders of the mentally handicapped population is to resolve the question of whether neuroleptic medication may contribute to motor disorders. We also agree that future studies on motor disorders of the mentally handicapped population should have a control group of similar population who have never been treated with neuroleptics.

Our pilot results from the dyskinesia screening project at the Cell Barnes Hospital (Kohen & Mathew, *Journal*, 1990, **157**, 621) show that 85.5% ($n=53$) of the 62 randomly selected residents rate positively by a score of two in at least one area of the body as defined by DISCUS (Sprague *et al*, 1989). Of the 37 subjects who are on neuroleptic medication, 86.5% ($n=32$) and of the 25 subjects who have never been on neuroleptics, 84% ($n=21$) have a motor disorder in at least one area of the body.

The neuroleptic medication is clearly not a necessary or sufficient cause for the motor disorder in this complex and varied institutionalised population. The next step will be to delineate the anatomical distribution of the motor disorders in a significantly large population and to attempt to subtype the different subsyndromes according to the usage of neuroleptics, overlay of psychiatric illness, chronicity of the illness, length of stay in hospital and other demographic characteristics.

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Engagement of relatives in intervention programmes

SIR: McCreadie *et al* (*Journal*, January 1991, **158**, 110–113) report on their attempts to engage the relatives of schizophrenic patients in an intervention programme. They found a disappointingly high level of refusal by relatives – just over half of those approached. In our experience, the timing of offers of help is crucial; we approach relatives while the patient is still in hospital with an episode of schizophrenia. At a time of crisis, which this represents, relatives are often desperate for help and welcome the offer of information about the illness. The process of engagement is greatly facilitated by the therapists' willingness to see relatives at home, and by a clear statement at the outset that the relatives are not viewed either as the cause of the illness or in need of psychological treatment themselves. The explanation we give for our intervention is "to help you to help the patient". This gets round the objection made by six of McCreadie's refusers that "it's the patient who needs help, not me".

Once the acute episode is over and the patient back home, the family rapidly returns to its routine and becomes relatively impervious to offers of help, as McCreadie and his colleagues discovered.

The authors acknowledge that their intervention was "an approximation of what was achieved in other studies", but it is impossible to tell how close or distant the approximation was since insufficient detail is given in their Brief Report. We are conscious that we have not produced a manual for our intervention, which would lay the groundwork for others to apply it clinicaly. However, we have run one pilot training course for ten psychiatric nurses of one and a half hours per week over nine months which has helped us towards creating a manual. It has also reassured us that the techniques can be acquired by clinical staff. Therefore, we do not share the pessimism of McCreadie and his group that professionals "in hard-pressed NHS psychiatric facilities" will not be seconded for this type of training.

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Patient data in child psychiatry

SIR: The contribution of Treffers *et al* (*Journal*, November 1990, **157**, 744–747) to the debate about the development of computerised databases in child psychiatry was welcome but in some respects misleading. The utility of such a system is determined largely by the extent to which it fulfils the clinical, administrative and research needs of a particular centre. The requirements of a teaching hospital department with extensive research interests will, of necessity, be different from those of the large number of clinical departments to which most patients relate. In the design of information systems, account must be taken of the need for flexibility to suit local needs (Sein, 1990). The demands of medical audit and management processes will call more for a common dataset between clinics which will facilitate cross-district and regional comparisons.

It is perhaps misleading to entitle a paper "Collecting patient data . . ." when, despite some well made general points about the issues, more than half the text is devoted to an exposition of an unvalidated and complex system of classifying family types. Useful though such an endeavour could be, it is exceedingly unlikely that such detailed demographic data collection would be economically viable as a routine feature of a clinical information system for child psychiatry in the National Health Service (NHS). In their introduction, the authors note that the development of information systems for child psychiatry has been slow. This is unsurprising since the impetus in the past has been predominantly research-based, necessitating such complex and detailed data collection as is described in this paper.

In the UK now a new impetus has been provided by the emphasis in the NHS reorganisation on systems for medical audit and monitoring of clinical activity. Small specialities such as child psychiatry may find it difficult to generate the resources to develop information systems which will 'travel' to other centres, although some pioneering systems have been installed in more than one centre (Berger, 1989; Byrne, 1989).

In order to meet these wider demands, databases need to be economical, efficient and relatively simple to use. If the authors' data-set is to achieve greater utility than that of a tool for epidemiological research then I suggest it will need piloting in several centres with careful evaluation, both of the scale of resources needed to support it, and of its usefulness within a scheme for medical audit.

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Child psychiatry liaison services

SIR: McFadyen *et al*'s descriptive account of the impact of a child psychiatry liaison service on patterns of referral (*Journal*, January 1991, **158**, 93–96) provides a timely impetus to this rapidly expanding area of child psychiatry.

While it is clear that the reorganisation of child psychiatric services resulted in a considerable increase in the number of liaison referrals, it may be useful to point out that there are other spin-offs from the provision of such services in paediatric units.

Our experience in Coventry suggests that senior registrar trainees in paediatrics, who are exposed to liaison services, incorporate some of the principles involved in those services and, subsequently, on obtaining consultant posts tend to value the contribution which child psychiatry can make to management of the psychological aspects of physical illness. This is in addition to helping to raise the awareness of nursing and other staff. We have noted that in the past six months the number of non self-harm referrals to the department of child psychiatry has virtually doubled since the appointment of a consultant paediatrician who has had training which was strongly informed by child psychiatry liaison services. This strengthening in the link with paediatrics, which we are currently monitoring prospectively, increases opportunities for involvement at many different levels beneficial to patient care.

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Beyond pumpkin seeds

SIR: We are interested in Eagles' letter (*Journal*, December 1990, **157**, 937–938) regarding the use of pumpkin seeds as a source of L-tryptophan, but suggest that there may be an alternative way of tackling the problem.

Since the withdrawal of L-tryptophan, a considerable number of patients previously receiving it have relapsed. In our experience, the time lapse involved has been between two weeks and two months after discontinuation. An answer to this seemed to be the reinstitution of L-tryptophan in a number of people on a named-patient basis. To this end we have generated a 'tryptophan monitoring clinic'. This is run with a multi-disciplinary team of doctor, nurse and hospital pharmacist. Supplies of L-tryptophan in the form of Optimax are available through the hospital pharmacy, via a signed request from the consultant in charge of each case.

The eight patients involved so far are all over sixty-five years old and have a long history of treatment-resistant depression. The majority are receiving lithium carbonate and a tricyclic antidepressant at therapeutic dosage with L-tryptophan as the third part of a triple therapy.

The clinic is held at the Day Hospital. Patients are seen for mental state examination, plus discussion of any risks and problems, by the doctor. There is also an opportunity for discussion with the nurse who takes blood samples to measure eosinophil counts. Monitoring of blood follows Committee on Safety of Medicines (CSM) recommendations and advice from the drug company. The pharmacist gives each patient personal information sheets relating to L-tryptophan and any of its potential side-effects. She dispenses sufficient supplies of L-tryptophan to last until the next clinic appointment (maximum one month). General Practitioners are informed that the patients are receiving L-tryptophan from hospital.

To date, improvement of mood is noticeable in all but one patient. In one hundred and forty-two patient weeks, four eosinophil counts have been very marginally above the normal laboratory range ($0.04–0.4 \times 10^9$/l). These have all reverted to within normal range at early re-test. No patients have shown any physical symptoms of eosinophilia myalgia syndrome.

We envisage continuing this service as long as the need persists. We have also started to see out-patients who are commencing L-tryptophan for the first time and for whom the consultant in charge feels this is the next step in their treatment programme.

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Blinding trials

SIR: I think the dispute between Newcombe (*Journal*, December 1990, **157**, 934–935) and myself (*Journal*, August 1990, **157**, 300) about the value of double-blind trials arises partly because of his idealistic view of the randomised controlled trial. The logic of the method is essentially unassailable, but I am more concerned with the real world of clinical practice. The problem of unblinding will not be solved merely by pleas for improved study design and execution.

Dr Newcombe's useful critique of the study by Karlowski *et al* (1975) fails to reach a practical conclusion about whether ascorbic acid is effective in the treatment of a common cold. Should we, therefore, take the advice of the Nobel Prize winner, Linus

Pauling (1970), with his regime of vitamin C to combat the common cold, based on his assessment of the evidence as a scientist?

Have clinical trials produced firm conclusions about the effectiveness of any treatment in psychiatry? If so, which are the methodologically sound studies? If not, considering the number of studies that have been conducted, would it not suggest there is an inherent difficulty in the design of the 'double-blind' method itself?

As an example, consider the evidence for the use of tricyclic antidepressants in depression in general practice. Hollyman *et al* (1988) found amitryptyline to be effective. By contrast, Porter (1970) found no difference between imipramine and placebo. Interestingly, Porter did not pretend his trial was double-blind, because he recognised that no trial of this kind can be conducted under completely blind conditions. In fact, he openly declared his bias that tricyclic antidepressants probably had no specific action in depression illness, although they may suppress anxiety and agitation by their sedative effect. He argued that his attitude towards the effectiveness of the drug might neutralise the influence of the breaking of the blind. The bias of Hollyman *et al* (1988) is less clear. Has their use of double-blind methods eliminated potential expectancy effects? It is a legitimate question. I am not suggesting it is easy to answer, but some evaluation may be possible with evidence from participants' guesses about medication status. An insistence on statistical purity in the analysis might produce a lack of awareness of the fallacy of the method.

The problem is that the results of 'double-blind' studies tend to be automatically accepted as scientifically valid. A misleading self-deception is encouraged that trials can be conducted double-blind, and the role of expectancies is underestimated. I understand the wish for a scientific basis for psychiatric treatment, but professional status should not mean that the challenge to double-blind methodology goes unnoticed (Oxtoby *et al*, *Journal*, 1989, **155**, 700–701).

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Demand for psychogeriatric services

SIR: We were interested to read the paper by Christie & Wood (*Journal*, August 1990, **157**, 228–231), and share the authors' concern over the failure to match resources to increasing demand, but wish to make two points. Firstly, from our own experience we doubt the findings can be easily generalised to other areas as the authors suggest and secondly, we are concerned that the problem of functional illness in old age may be overlooked because dementia so preoccupies the debate about the ageing population and service provision.

We have had 336 admission episodes (over the age of 65) during the past two years of which 44% were dementias (34% excluding planned respite care), 33% affective disorders, 12% schizophrenias (early and late onset), 1% acute confusion and 10% other conditions, mostly adjustment reactions or medical problems. Christie & Wood report an astonishing 76% of their admissions to be dementia and only 16% functional illness, whereas over 45% of our episodes were functional, over 53% if dementia respites are excluded.

Accepting that the Crichton Royal study only included patients over 69 years of age, these differences are considerable. Christie & Wood cite similarities between Blessed & Wilson's Newcastle study (*Journal*, 1982, **141**, 59–67) and the early Crichton Royal study (Christie, *Journal*, 1982, **140**, 154–159) – both performed in the mid-1970s – as evidence that their findings are of more than parochial interest. However, the Newcastle admission rates more closely resemble our own than the Crichton Royal data at that time with 41% functional, 43% dementia (Newcastle) and 29% functional, 50% dementia (Crichton).

These differences may reflect widely-differing clinical practices, varying illness prevalence, different community provision, social and family support or other factors that distinguish deprived city catchment areas like Liverpool and Newcastle from rural areas like South-West Scotland. Without far more information about these variables it is difficult to interpret the Crichton Royal findings or see how they may translate to other areas. The requirement for long stay dementia beds, for instance, depends on several variables (Blessed, 1988), including the provision of residential care, and the private sector contribution to this varies eight-fold nationwide (Joint Colleges' Report, 1989).

Contrary to the experience at the Crichton Royal, our major difficulty is providing in-patient beds for the functionally ill, which again may be a local problem. Functional patients will always require in-patient services while one could argue that the long-term care of dementia need not, or should not, be in a hospital ward. We no longer have long-stay dementia beds and it seems highly likely that all areas will find their long-term care beds being dismantled. Our concern is that while we pursue a largely futile case for more long-term dementia beds, the problem of acute functional illness may be forgotten.

Functional illness remains more prevalent than dementia, active psychogeriatric services generate increased demand for in-patient treatment for functional illness (Joint Colleges' Report, 1989) and the 'graduate' population in the community continues to increase. This will inevitably drift into the psychogeriatric domain and may prove a considerable drain on resources. It will be a mistake to underestimate the future demands of functional illness in old age.

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How old are the elderly?

SIR: I read with interest the paper by Cook *et al* on depression and previous alcoholism in the elderly (*Journal*, January 1991, **158**, 72–75). The majority of psychogeriatricians in the UK deal with clientele above the age of 65, and in some cases the age limit goes to 75. Interestingly, the authors consider subjects above the age of 55 as elderly and the mean ages for subjects with alcoholism and no alcoholism were 57.7 years and 62.5 years respectively. Probably this reflects the differing views of what age is considered as being elderly?

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The 'new cross-cultural psychiatry'

SIR: Professor Leff has the advantage of having his letter (*Journal*, December 1990, **157**, 932–933) published in the month following mine. My own letter (*Journal*, November 1990, **157**, 775–776) languished somewhat after its submission in March and the original argument may no longer be so fresh to readers of the Journal. In his editorial preceding my review of the 'new cross-cultural psychiatry' (Leff, *Journal*, March 1990, **156**, 305–307; Littlewood, *Journal*, March 1990, **156**, 308–327) Leff made a number of errors of fact and interpretation, to two of which he replies.

My point on the 'existence' and gender of smallpox deities was essentially factual. Professor Leff answers more generally on evaluative questions, inevitable for a pragmatically-orientated psychiatry as opposed to a more distanced if nuanced anthropological position. I am far from certain that "an anthropologist is neutral as to whether or not people die of smallpox"; I for one am not. As I described in my paper, clinically-applied anthropology, including understanding of local beliefs about sickness, is now a part of the provision of clinical services (Chrisman & Maretzki, 1982; Kleinman, *Journal*, August 1990, **157**, 295–296), a development which both of us appear to value.

The fundamental difference between the two disciplines seems now to be one of the degree of 'objectivity' claimed. Neither, of course, are context-independent reflections of some transcendental reality existing independently of our procedures of observation, but it is interesting that social anthropology, once regarded by biomedical science as somehow dealing in 'soft' data, seems here to have acquired a harsher objectivity (cf. Clifford & Marcus, 1986) in a way psychiatry has not, conflating as it does fact and value whilst mistaking the latter for the former. There is an irony here in that disciplines which allow for observer bias suddenly seem to switch from extreme subjectivism to super objectivism.

I would, of course, hardly quarrel with Leff's restatement of the value of our examining local meanings before carrying out comparative studies. Indeed this may be taken as the central 'motif' of the 'new cross-cultural psychiatry' (Kleinman, 1977). Nor would one be surprised that this procedure might not prove to be feasible, either for economic, organisational or ideological reasons. But our failure to carry out a study of local contexts must be accompanied by an appreciation of the limits of the data we can collect without it. Inevitably, a purely epidemiological study employing diagnostic criteria derived from one society alone will lead to our 'conventional error'. Attempting to remove culture from the whole study initially to control for it as an independent variable later leads to a fictitious construction of the whole field, in which culture is simply subtracted from psychopathology leaving our phenomena of interest simply as an ill-connected assortment of biological, psychological and social variables. Our failure to provide plausible explanations for the cross-national prognostic differences in the International Pilot Study of Schizophrenia is a striking instance.

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This correspondence is now closed. I.P.

Informed consent in India

Sir: The ethical issues raised by the concept of informed consent for medical procedures are complex. The controversies have mainly arisen secondary to the choice of the standard employed. The two criteria commonly used have been individual freedom (and the patient's right to refuse treatment), and society's right (and the related right to therapy), which are often mutually exclusive. The western world has tended to favour individual rights when the patient's 'competence' is intact, while it takes over decision-making when this faculty is considered impaired. The implementation of the ethical criterion is thus dependent on the clinical situation and represents a compromise. Electroconvulsive therapy (ECT) has been given a special status among treatments and hence requires specific consent. Although informed consent and true voluntarism are ideals, in reality they are rarely attained, as such decisions contain an element of coercion, ranging from subtle to overt (McGarry & Chodoff, 1981). Thus, in practice, the ethical choices are difficult.

In India, this decision is further compounded by the existing socioeconomic and political realities. The majority of patients, being illiterate and poor, are unaware of their individual rights or the issues involved and may not comprehend the significance of the explanations offered. In addition, the doctor–patient relationship commonly viewed within a 'guru–disciple' context leads to a situation where the physician decides for the patient. Informed consent against this background tends to become a formality.

Consent for ECT as generally practised is part of the general implied consent to treatment given at the time of seeking therapy, although a proportion of psychiatrists would, from the legal point of view, recommend specific consent as mandatory. This stand may be ideal for the educated classes who are aware of the issues involved, but it does not alter the position of the majority of the patient population, as it would only comply with the letter rather than the spirit behind consent. Blindly adopting western standards in regions where the ground realities are not comparable would be a pretence.

The ethical answer to this complex situation has to be found within the social context of the society. The prevalent culture in India, and hence the majority, is inclined to attach more importance to health than to individual autonomy. Thus, the physican would have to assess the patient's value system and priorities and if health is considered cardinal, the decision to use ECT, despite it being the physician's choice, may be ethically justified. Similar arguments have been employed in the West to support the use of the placebo in treatment where the fiduciary nature of the physician–patient relationship is violated in order to retain its therapeutic aspect (Kluge, 1990). Obtaining informed consent for the use of the placebo would imply that its therapeutic aspect is abandoned. In such contexts, the ethical decision would be dependent on the physician and this would be part of his burden of caring for patients. Although simple explanations about the procedure should be offered, in the prevalent circumstances this by itself would not necessarily satisfy the spirit of informed consent. Informed consent obtained on paper may provide legal protection to physicians but it certainly would not take away the moral responsibility and in fact adds to the ethical dilemma. Similar situations probably exist in many third world countries for which medical interventions and ethical solutions would have to be found within the socio-cultural context.

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Clozapine-treated NMS

Sir: Having recently experienced difficulties treating a floridly disturbed young schizophrenic man who had previously had two episodes of neuroleptic malignant syndrome (NMS), we felt it may be helpful to others in this predicament to report our experience with clozapine.

Case report. The patient was a 35-year-old man with an 18-year history of schizophrenia, which for some years had been resistant to a broad range and dosage of established antipsychotics, therapeutic only in that he was a little more in touch with reality and his behaviour rather less disturbed. He had needed several periods of treatment in the secure unit, for unprovoked assaults in his District General Hospital ward. He was receiving treatment with zuclopenthixol (1000 mg weekly), chlorpromazine (200 mg q.d.s.), and procyclidine (5 mg t.d.s.) when he developed NMS characterised by pyrexia, rigidity, flushing, sweating and agitation with some apparent confusion. Creatine phosphokinase (CPK) levels were significantly elevated (up to 1467 IU/L). His antipsychotic medication was stopped and the NMS abated. He remained settled for a number of weeks but his psychosis returned and required treatment. It was felt that chlorpromazine was worth trying cautiously, but he developed a recurrence of NMS, and all antipsychotics were stopped. Following recovery from NMS, his mental condition deteriorated rapidly with florid delusions, severe thought disorder, and grossly disordered behaviour and aggression, necessitating transfer to the secure unit and treatment in seclusion for an extended period. General sedation with phenobarbitone and benzodiazepines was unsuccessful. We were faced with a difficult dilemma, in that he needed urgent antipsychotic treatment but stood the risk of recurrence of NMS. In view of the recurrence with chlorpromazine, it was felt that most of the well-established drugs were not acceptable (Susman *et al*, 1988), and in view of its different chemical structure and pharmacological profile (Coward *et al*, 1989), a decision was made to commence the patient on clozapine, with the usual precautions, plus observations with a view to detecting NMS. Over a period of seven weeks the patient improved markedly in behaviour, thought and contact with reality, and regained some of his emotional warmth. He is as well as he has been for several years, has shown no signs of a recurrence of NMS, and is well enough to return to the open ward.

Apart from being consistent with reports that clozapine is effective in resistant cases who have not responded to other established medication (e.g. Kane *et al*, 1988) this case suggests that clozapine is a drug to consider when a patient has suffered NMS.

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All-night television can damage your health

Sir: Patients with chronic schizophrenia often reverse the more usual night/day pattern of sleep and activity. This enhances their social withdrawal and hinders attempts to engage them in rehabilitation programmes. The provision of all-night television on the independent channels since August 1987 reinforces this behaviour and can have deleterious effects on the mental states of patients if, as a result, they fail to comply with, or attend for, medication. The following case report illustrates how all-night television watching led to a self-limiting symptomatic relapse.

Case report. A 31-year-old Afro-Caribbean male who lived with his parents and sister and who had a 10-year history of paranoid schizophrenia was symptom-free on a weekly depot and twice-daily oral anti-psychotic medication. He attended a day hospital where he received his medication and attended workshop facilities. His generally excellent attendance at the day hospital declined and he regularly missed the mornings, arriving between 1.00 p.m. and 3.00 p.m., complaining of feeling tired. Under close questioning he admitted that he had started watching all-night television until 5.00 a.m. He missed doses of his prescribed oral medication and for some weeks he also missed his depot and started to complain of unpleasant auditory hallucinations. When confronted with his poor attendance and compliance and advised to go to bed earlier so that he could attend a full day at the day hospital, he refused, saying that he enjoyed the selection of programmes available overnight and was not prepared to miss them. After six weeks of poor attendance and missing doses of medication he began to experience auditory hallucinations emanating from his television set, and to feel that people on television were interfering with his thoughts. These experiences made television watching intolerable and, consequently, he began to retire to his bed earlier. His attendance at the day hospital improved to that his prescribed medication could once again be given under supervision, and his symptoms disappeared.

When patients with day/night reversal fail to attend out-patient or day hospital facilities, or sleep through their medication times, enquiries should be made as to how the individual is spending his nocturnal waking hours. If a fondness for all-night television contributes to the problem, appropriate counselling can be tried but may fail, as in this case. Perhaps the television companies should strive to improve the quality of broadcast material during normal waking hours!

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Toluene-related psychosis

SIR: Further to previous correspondence on this subject (*Journal*, 1989, **155**, 132), we would like to address the issue of toluene-related psychosis in the context of solvent abuse. The patient cited in the history below has previously been mentioned in your columns, as he has frequently required treatment for psychotic symptomatology related to inhaling adhesive mixtures.

Case report. A young native Canadian male was readmitted to our unit in a dishevelled state, having been found wandering by the local police. At interview he was disorientated and tremulous, and displayed oculogyric symptomatology. He could give no history at that time. His clouded consciousness precluded full mental state evaluation. He was commenced on chlorpromazine (50 mg twice daily), and benztropine was administered to control his oculogyric symptoms.

The patient settled quickly, and within 72 hours his behaviour was quite appropriate at interview, showing no signs of paranoia or disorientation. He revealed that he had changed his brand of solvent, and was now inhaling paint-thinner instead of adhesives. He was fit for discharge within one week of admission, is currently abstaining from solvent inhalation, and is on no medication.

It is notable that this patient settled so quickly on this admission, having previously required months of hospital treatment for episodes of paranoid psychosis related to solvent abuse. The solvent he inhaled prior to this admission was acetone-based, and his clouding of consciousness was short-lived. The inhalation of toluene-based adhesives had previously produced a definite paranoid psychosis in this man, but no such condition was evident on this admission. We suggest that toluene was the agent responsible for the paranoid psychosis in his case; the lipophilic nature of the substance, and its slow excretion from brain tissue, producing a much more protracted cerebral disturbance. We feel that toluene inhalation was a cause of paranoid psychosis, and that extensive inhalation may have major neuropsychiatric consequences.

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A HUNDRED YEARS AGO

Music as a remedy

Most of us have at one time or another been convinced by personal experience of the fact that perception of pain and of grief depend in great measure on our mental attitude for the time being. It grows under observation, wanes if neglected, and is even obliterated for a time if our emotions are strongly acted on by some shock or counter attraction. It is clearly in this way that we must explain the anaesthaesia of hypnotism and the soothing effects of harmony in sound. This very sense of calm has, moreover, as a form of rest, a distinctly curative tendency, so that music may to this extent be regarded as a remedy in illness. The ancient healers understood this, and we find accordingly that hardly any prescription or course of treatment was by them regarded as efficacious unless agreeably combined with the allurements of melody or quaintly blended with an incantation. Egyptians, Indians, Greeks, and Romans in turn wooed in this manner the *vis medicatrix*, and, we cannot doubt, with a fair measure of success. It need hardly excite comment, therefore, that the same attraction of melody has been credited in our own days with a curative property. One of the latest notes on this subject is one which applauds music as an anodyne in gout. The reference, of course, is to the pain endured rather than the malady which occasioned it. This latter is beyond the control of merely neurotic forces. What refinements of molecular change in the sensorium underlie the anaesthesia so readily induced there is as yet no evidence to show. Whatever their nature, however, we may take it for granted that they do occur, and the process which gives rise to them is perhaps not altogether unworthy of experimental use now and then by the modern practitioner.

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Lancet, 25 April 1891, 951.

Research by Henry Rollin, Emeritus Consultant Psychiatrist, Horton Hospital, Surrey

British Journal of Psychiatry (1991), **158**, 579–582

Reading About . . .

Transcultural Psychiatry

The perspective for this review is that of a general psychiatrist who is convinced of the clinical relevance of sociocultural psychiatry for a full, multimodel understanding of mental illness, and is aware of the intellectual stimulus which occurs when the clinical and research vistas extend from one cultural unit to another (i.e. *trans*cultural psychiatry). My specific purpose therefore is to name some books which can help establish 'good practice' in multicultural Britain and are useful reference texts for teaching, as well as research. The choice of books inevitably reflects my own clinical and academic interests, and the volumes received from the review editor of this Journal over recent years. Any particularly disenfranchised reader will nevertheless find sufficient reference to other aspects of this fascinating field which has now become central to much present day clinical practice; transcultural psychiatry has been regarded as having 'come of age' and yet paradoxically also as beginning 'at home'. Evidence in support of these developmental aphorisms can be culled from the publication of at least 20 books on cultural psychiatry in the last two decades, as well as from the final reports of the World Health Organization epidemiological studies which may have reassured the dubious that the major psychoses, such as schizophrenia and manic–depression, and even the neuroses are universally recognised, even if their presentation and 'explanatory models' differ radically between some cultures, although are similar in others.

Thus the academic and clinical aspects of transcultural psychiatry have now achieved a respectability and popularity which is somewhat surprising because 15 years ago some prophesied its early demise, and doubted its relevance to psychiatrists working in the UK. Moreover, at the present time, courses on transcultural psychiatry are recommended in the new code of practice for the Mental Health Act and as part of the required training for approved social workers. Our own College, in an impressive way, has recently endorsed most recommendations of a subcommittee that such teaching is a necessary component of general, higher and, as important, of continuing medical education for consultants.

Historical aspects

Although Murphy (1986) was presumably correct in suggesting that one of the first writers to link culture and mental health was the 14th-century Arab social historian, Ibn Khaldun, who noted a growing prevalence of jealousy, distrust and self-indulgence when warriors moved from a nomadic, supportive village to a town, it is Murphy himself who many would regard as a founding 'father' of transcultural psychiatry. His scholarly book *Comparative Psychiatry: the International and Intercultural Distribution of Mental Illness* (1982) gives particular emphasis to research methodology (which is primarily epidemiological), and illustrates the specific advantage of investigating *subcultural* differences within national and ethnic groupings. The book is not easy reading and may be complemented by Leff's smaller and attractively published new edition of *Psychiatry Around the Globe* (Leff, 1988), which also draws inspiration from research findings and yet illustrates the limitations of much transcultural research. To an extent the book begins to answer the questions asked by Leff as to whether psychiatric conditions are similar in different cultures, what their frequency is and whether they are treated differently. The second edition is less ethnocentric than the first, and the section on linguistic aspects of somatisation has been largely rewritten; there is a greater emphasis on the pitfalls of the 'category fallacy' – the imposition of a Western diagnosis on a non-Western society with the risk of missing important local manifestations and managements of psychiatric disorder.

Kleinman (1980) elaborates extensively on these diagnostic traps and his books are particularly important for a general psychiatry readership. Kleinman, psychiatrist and social anthropologist (although primarily perhaps the latter?), brings to his thinking not just a social critique of psychiatric diagnoses, but a description of the relevance of social anthropology for eliciting 'explanatory models' of patients – including those seen by a liaison psychiatrist in a general hospital setting. He draws substantially on his own field work in Taiwan and is well known for his detailed critique of the causes of somatisation in the Chinese.

Murphy, too, was aware of the conceptual tensions within transcultural psychiatry, and in particular of the assumption that it has to do with minority groups only, or with societies in exotic parts of the world. He pointed out to me that the initial list of contents for the book *Transcultural Psychiatry* (Cox, 1986) contained only limited accounts of the Irish, the Welsh or the Scots and he therefore offered to write the additional chapter "Mental health impact of British cultural traditions". This probing attitude was characteristic of his scholarship, and has underpinned the McGill Transcultural Psychiatry Centre and the *Transcultural Psychiatric Research Review* – one of the foremost journals in the field. It was Murphy's own dictum that 'transcultural psychiatry' began at home, and his account of the relationship of British culture to psychiatric disorder, although restricted to the subculture of the Brits abroad, was his attempt to practice what he preached. When will someone write the ethnography of the English at home, I wonder?

It is to the writings of Littlewood (psychiatrist and anthropologist) and Lipsedge (a general psychiatrist) that we should turn for further discussion of the need to develop a local cultural understanding of psychiatric disorder, and for an awareness of transcultural psychiatry as a cogent critique of Western diagnostic concepts. In their popular book *Aliens and Alienists* (Littlewood & Lipsedge, 1982), now in its second edition, the cultural assumptions sometimes linked to prejudiced attitudes of much clinical psychiatry are pointed out. The book is hard-hitting and yet never damagingly antipsychiatry. These authors are prolific in their writing, which is always concentrated (see, for example, their review chapter in *Recent Advances in Psychiatry* (Littlewood & Lipsedge, 1985)), and yet can be recommended for the reader who is prepared to read around social anthropology and is particularly interested in alternative understandings of descriptive psychopathology or who wants access to the literature. Their chapter, "The culture-bound syndromes of the dominant culture: psychopathology and biomedicine" (Littlewood & Lipsedge, 1986) includes a fascinating discussion of anorexia nervosa as a western culture-bound disorder linked to feminist dilemmas; parasuicide through overdose is regarded as an appeal to the dominant biomedical paradigm (i.e. the drama of the casualty department) – which medicalises a social crisis, and requires biomedical expertise if the outcome is to be what was initially intended.

Clinical aspects

What texts can be recommended for a psychiatrist who wishes to be equipped for 'hands on' sector psychiatry in a multicultural, multiethnic environment – perhaps most consultants working in the city areas at the present time? This writing can only be undertaken by pragmatic clinicians providing community clinical services with scarce manpower resources, and Rack's (1982) *Race, Culture and Mental Illness* is therefore the best buy, particularly for his informative account of the pioneer multicultural service at Lynefield Mount Hospital, Bradford and for his matter-of-fact approach to the daunting clinical tasks which he faced. It is a reliable handbook for those wishing to be reminded of the pitfalls of psychiatric provision to minorities – especially when being provided by a psychiatrist from an ethnic majority, as well as of the 'orders' of difficulty which such provision entails, such as language problems, diagnostic pitfalls and the hidden cultural assumptions of the psychiatrist. A close runner-up, however, is *Race and Culture in Psychiatry* by Fernando (1988). This is especially convincing writing, not just because it is from an author who feels what he writes and includes chapters on racist psychiatry and cross-cultural research, but also because it puts forward the interesting concept of sociocultural psychiatry and in its final chapter looks constructively at the possibility of how positive changes can occur in clinical practice and in personal attitudes, and gives advice as to how this change can be brought about. Fernando (1988) has a particularly shrewd insight into the causes of depression in ethnic minorities and of the way in which discrimination may poison the person, form a threat to self-esteem, and yet can be counteracted by new coping strategies.

These texts rightly emphasise that the psychiatrist in multicultural Britain is required to understand the 'language' used by patients and needs a sensitivity to the effect of individual and institutional discrimination on their Mental Health.

Such issues are not, however, confined to psychiatry, and Quereshi's (1989) *Transcultural Medicine: Dealing with Patients from Different Cultures* and Henley's (1979) *The Asian Patients in Hospital and at Home* includes much information relevant to general physicians who are short of facts about the beliefs and customs of minorities which would limit the effectiveness of their clinical practice.

It is nevertheless to authors with particular experience of two cultures, such as Bavington & Majid (1986), that one might turn for a particularly authentic account of the provision of psychiatric services for minorities. Their writing can therefore be recommended, as can many of the chapters in *Between Two Cultures: Migrants and Minorities in Britain* (Watson, 1977). This latter text describes how some ethnic minorities retain links with their home culture, and so experience some aspects of the psychology of the sojourn. Krausz (1972) and Wilkinson (1986) also include useful information about the history and customs of ethnic minorities in Britain and the US respectively, including their sociocultural similarities to, and differences from, the majority society. The account of the Polish and Greek Cypriot communities was of particular interest, as was the description of mental health problems of Asian Americans, and Pacific Islanders.

Teaching and research

While there are several American books which have included information about course programmes in transcultural psychiatry, there is little specific guidance available for tutors in the UK. There is a definite need for such a book to be written. *Cross-Cultural Psychiatry* by Gaw (1983) has a section on cultural issues in psychiatric residency training, and outlines the course content for a three-year training programme. It has a short section on experiential training methods which are so vital to good learning of this subject. Marsella & Pedersen (1981) in *Cross-Cultural Counselling and Psychotherapy* also emphasised the need for experiential teaching and for personal insight into the cultural background of the therapist, as well as the client. Tseng & McDermott's (1981) *Culture, Mind and Therapy* includes a fascinating account of the psychology of intermarriage and has advice for marriage counsellors, as well as a section on research and training. They clearly recognise that the psychiatrist has to be informed about culture and the anthropologist needs to understand clinical psychiatry. This is a theme also discussed in depth by Kleinman & Good (1985) in their *magnum opus, Culture and Depression: Studies in the Anthropology and Cross-Cultural Psychiatry of Affect and Disorder*. Good shrewdly brings together anthropological/psychiatric perspectives by advocating that the anthropologists should examine critically their own assumptions about the differences between disorders of the body and of the mind (physical disease is culturally interpreted while mental disorders are culturally produced) and should not ignore the potential power of conceptualising depression as a disease. Medical-anthropological studies he suggests are optimally carried out in "clinical settings" and by a conjunction of different case-finding techniques and epidemiological methods. Such research collaboration is difficult but Rubel *et al* (1984), in their study of *Susto, a Folk Illness*, show how this can be brought about, although it was a disadvantage that a psychiatrist was not a member of the team. Nevertheless this text is an excellent attempt to describe the local concepts and the phenomenology and causation of *susto* (soul loss) and to look for the way it may include physical and psychiatric disorders recognised by physicians.

Interface between psychiatry and anthropology

For medics wishing to enter the world of the medical anthropologist the text book by Helman (1984) is most readable, and now in a second edition. It includes a section on transcultural psychiatry, as well as on cultural aspects of stress. The discussion draws its source material from the medical pluralism in Great Britain, and on the implications of this for the delivery of health care. Beattie's (1964) paperback *Other Cultures: Aims, Methods and Achievements in Social Anthropology* is a well written account of social anthropology which a non-anthropologist can readily grasp. His discussion of 'stranger value' I found particularly helpful when considering the limitations of my own research in Uganda. More complex books about medical anthropology include those by Loudon (1976), Chrisman & Maretzki (1982), Foulds *et al* (1977), Eisenberg & Kleinman (1981) and Galdston (1971).

Finally, I shall conclude this review with a brief mention of those books which I have found particularly helpful when working between two cultures and to which I frequently refer with sustained interest, as well as legitimate nostalgia.

The book based on the prestigious CIBA symposium (de Reuck & Porter, 1965) was one of the few available on transcultural psychiatry at that time, apart from Kiev's (1972) text; Lewis, who chaired the symposium, repeatedly emphasised his belief that a 'fruitful' collaboration was possible between psychiatrist and anthropologist. Indeed, such pioneers as Margaret Mead, Morris Carstairs, T. A. Lambo, E. Wittkower, Alexander Leighton, Yap and H. B. Murphy attended. The verbatim discussions are vivid and controversial, as shown in Yap's chapter, "Affective disorder in Chinese culture", which also has clear figures linking psychopathology with cultural variables. Orley's (1970) *Study from Uganda: Culture and Mental Illness* should also be reprinted and available in most libraries. It represents the distillation of intensive field work among the Baganda uncovering their own concepts of neurosis; participant observation at its most relevant to academic and clinical psychiatry. Indeed it enabled Orley to translate the Present State Examination into Luganda and also to pass on his self-confidence to many of us who then undertook similar research. *Culture Shock* (Furnham & Bochner, 1986) is relevant for any researcher interested in understanding the psychology of adjustment disorders – a subject still under-researched by psychiatrists and yet of much clinical relevance. It is a lucid text with an excellent bibliography – a good handbook for a traveller. Finally I recall avidly reading Carstairs & Kapur's (1976) *The Great Universe of Kota* – while on holiday in Scotland. The research methods grappled with the relationship of psychiatric disorder to different sections of Indian society, and in so many respects succeeded in testing a transcultural hypothesis using behavioural science method.

For the reader who may not have the prolonged opportunity to study social anthropology (and yet would like to), the account of culture by Lewis (1976) is a good introduction to the subject and would certainly whet the appetite for more. I shall therefore end this review, appropriately, with a quotation from that book which makes so clear the relevance of social anthropology and culture to sector psychiatry, and illustrates the enviable ability of some social scientists to communicate clearly to another discipline.

> "For our purposes culture is simply a convenient term to describe the sum of learned knowledge and skills – including religion and language – that distinguishes one community from another and which subject to the vagaries of innovation and change, passes on in a recognisable form from generation to generation. Culture thus transcends the lives of its living exponents in any one generation; if it did not it could not survive. Its component elements are absorbed in the first few years of life largely unconsciously and later more deliberately by informal and formal learning processes. Socialisation inevitably takes place within and through the medium of a particular cultural tradition. When people do not know how to bring up or what to teach their children, their cultural heritage is indeed in jeopardy."

Transcultural psychiatry, this reviewer believes, has now not only come of age but is approaching rapidly mid-life and the productive 'middle aging' generativity phase.

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Book Reviews

Editor: Sidney Crown

Perspectives on 'Hysteria'. By PHILIP R. SLAVNEY. Baltimore: Johns Hopkins University Press. 1990. 220 pp. £17.50.

Dr Slavney regards hysteria as a confusing concept and a word which is likely to disappear from current usage. He explores how thinking in terms of diseases, dimensions of personality, goal-directed behaviour, and life stories can help resolve the question whether 'hysteria' refers to something a person *has*, *is*, or *does*. He concludes that hysteria is not something which a patient *has* but rather reflects something a patient *is* and something a patient *does*. Why patients are what they are and do what they do, is a question which he thinks should be answered through meaningful interpretations of the life story, which may be conflicting and inconsistent.

This argument is developed for good reason. Hysteria has been a controversial concept and the meaning of the word has changed over the centuries. Modern psychiatry has effectively dismembered it into three major sections. One is the vernacular use of the word to indicate noisy or excited behaviour. The leading use today, is for a symptom which solves a conflict. The third notion is that of the hysterical personality, which has been inherent in the literature for nearly 200 years, if not longer, but which only began to be well specified in the last 50 years or thereabouts.

The book begins with introductory chapters which cover the initial reified concept, the obligatory historical reference to uterine theories, and the equally obligatory mention of Sydenham and similar workers. This is followed by a recognition that it was not possible to build up the notion of hysteria from physical findings and hence it began to be seen as a concept which should be treated descriptively with *post hoc* interpretations. There is a perceptive and understanding treatment of the notion of somatisation disorder with an explanation of the disadvantages and the importance of this concept in the development of modern ideas. There is also a very skilful demonstration of a sad case history and the way in which mature understanding of the case led to highly sensitive and useful management of the patient. Slavney explores, at relative length, the understanding of dimensions and traits in relation to hysteria. He is particularly strong in this respect, having made significant contributions to the field. Other topics include items like the sick role and life-story perspective, mentioned already, and also some comments on Anna O, and the other cases of Breuer and Freud.

This is a worthwhile and eminently reasonable volume. It is not comprehensive but it is a valuable contribution, indicating the way modern thought has evolved about some of the fundamentals of the topic and demonstrating, incidentally, how best such patients may be cared for.

HAROLD MERSKEY, *Professor of Psychiatry, University of Western Ontario, London, Ontario*

Other Times, Other Realities. Toward a theory of Psychoanalytic Treatment. By ARNOLD MODELL. London: Harvard University Press. 1990. 180 pp. £21.95.

Psychoanalysis is frequently regarded as a quaint anachronism by British psychiatrists. Psychiatric trainees are rarely exposed to serious and sensible teaching in this area, and the important contribution to ideas which psychoanalysts have developed over the years is more often than not ignored. Instead, a pastiche of miscontrued and oversimplified caricatures of Freud's early writing is presented. The verbose productions of some analysts and the gnomic intimations of others have not helped.

Modell provides a welcome antidote to this unfortunate state of affairs. He presents an elegant synthesis of modern thinking in the field, repolishing old conceptual lamps so that they shine with new meaning.

Old and false dichotomies such as the distinction between 'transference' and 'real' relationships have given way to a complex vision of multiple *levels of reality*, each acting upon the other and transforming it. The therapeutic relationship is jointly constructed in the consulting room, driven not by the dark forces of repetition–compulsion rooted in instinct, but the need to reconstruct and retranscribe perceptual categories.

This squares with Edelman's view of what is stored in memory as – the potential to activate categories of experience. Memories, like original perceptions, have to be constructed, they are not simply given by external events and waiting to be retrieved on a store-room shelf.

In fact Freud's concept of *Nachträglichkeit*, translated by Strachey as 'deferred action', is held by Modell to be better construed as – the notion that memory is retranscribed in accordance with later experience.

In this view the therapeutic potential of psychoanalysis is recast from the old saw whereby id is rendered into ego. Instead a transformation of inner reality is seen to take place, in the medium of the psychoanalytic setting through symbolic actualisation. Time is retranscribed in order to overcome the 'tyranny of the past'.

Psychoanalysis is shot through with paradox, not least the tension between the correspondence theory of truth which suggests that objects can be known *as they actually are* and the coherence theory with its emphasis on objects *as they are constructed.* Modell's argument is an eloquent exposition of the problem.

STEPHEN WILSON, *Consultant Psychiatrist and Clinical Lecturer, University of Oxford*

Dimensions of Psychoanalysis. Edited by JOSEPH SANDLER. Madison: International Universities Press. 1990. 263 pp. $35.00.

Psychiatrists who equate modern psychoanalysis with Freud's contribution alone are invited to a display of some of the harvest fruits of post-Freudian psychoanalysis. The volume mostly consists of the addresses of Visiting Professors of the Freud Memorial Chair at University College London, which celebrated its 25th birthday in 1990. It is introduced by Sandler, the editor and first long-term holder of the chair.

The addresses were to general audiences. However, non-specialists in the field may well wish to start with a lucid summary of Freud's early work by Gillespie, and then turn to Solnit's stimulating address on the significance of memory for attaining mastery and coping, and on preparing for the future with its potential for traumatic experiences. After Solnit, the reader could turn to Shafer's striking attempt to demystify theory and practice, namely by translating the analysand's life-history into 'action' language, and his or her unconscious defences into personal activity.

Those concerned with the scientific status of psychoanalysis will be interested in Bowlby's clear address on "Psychoanalysis as a natural science" and his robust theory of motivation which differs radically from that of Freud, and Pibram's attempts to provide a frame within which psychology, psychiatry and psychoanalysis can conform to the natural sciences.

Short dips into other lectures help to identify the book's challenging range. Green postulates a tertiary process of rationality, which bridges both primary and secondary processes of thought and logic, by a compromise which the analyst has to decipher. Segal reminds us that freedom of thought includes our knowledge of bad as well as good thoughts, a freedom we lose when external authority makes us afraid to speak, or internal authority (the superego) afraid to think. Klauber exposes the role of truth and illusion in transference and in psychoanalytic cure. He views transference illusion or delusion not simply as false perception, but as the similarity with, and the confusion of, an old relationship with a new. Chassueget-Smirgel skilfully reveals perversion as man's universal temptation to go beyond the narrow limits of his condition, to discredit the power of universal laws and the Father-Creator. Lasch, a professor of history, challenges the Freudian left, and their assumption that the patriarchal family is the source of organised oppression.

Finally, Sandler warns us of the gaps and weaknesses in psychoanalytic (as in all) theories. He persuasively invites those who have not done so, to move from the older mechanistic psychoanalytic structure to a model centred on an internal object-relational structure, an inner-world of self interacting with valued people.

These are valuable contributions to a crucial and steadily evolving discipline and will excite a surge of interest in those wishing to update their knowledge of the past.

BRIAN LAKE, *Honorary Consultant Psychotherapist, St James's University Hospital, Leeds*

International Perspectives in Schizophrenia – Biological, Social and Epidemiological Findings. Edited by MALCOLM WELLER. London: Libbey. 1990. 227 pp. $40.00.

This book has over 50 eminent contributors and provides a comprehensive and up-to-date review of schizophrenia. It is divided into five sections: the biology of schizophrenia, genetics, epidemiology, new directions in pharmacology and social aspects. Recent research findings and current reviews of the literature are provided in many chapters, although some of the summaries would have been of greater help if they had been more comprehensive.

The first section critically examines the time-honoured concept of schizophrenia as a functional disorder and includes contributions on organic 'schizophrenia-like' psychoses, memory in schizophrenia, developmental precursors of the adult disorder and the association between epilepsy and chronic psychosis. The significance of genetic factors in aetiology is reviewed in the second section along with molecular genetic research into schizophrenia and the search for psychophysiological changes (such as eye-tracking dysfunction) as biological markers for the condition.

The epidemiological section considers the interaction of environmental and endogenous factors in schizophrenia, and there is an overview of the Nithsdale schizophrenia surveys and the Friern Hospital studies which looks at the implications for community care following the intended closure of a London psychiatric hospital. New directions in pharmacology includes excellent chapters on drug-induced akathisia and tardive dyskinesia and new possibilities for drug treatment of schizophrenia. I especially enjoyed the final section on social aspects, in particular Falloon's chapter on family management of schizophrenia.

In common with other multi-authored books, a wide variation in writing styles gives the book a rather disjointed and lumpy feel, and in terms of layout, it is not particularly 'user-friendly'. Some of these problems could have been overcome by more imaginative and skilful editing. Overall, I found it rather heavy going and pedestrian in style, very much a book for reference purposes rather than bed-time reading. It is most suited for the postgraduate with a substantial baseline knowledge of the subject, and I would hesitate to recommend it, for example, to candidates preparing for the Membership exam.

Apart from a few niggling gripes, it tackles the various issues concerning the aetiology, diagnosis and management of schizophrenia in a business-like but uninspiring fashion. Unfortunately, the most entertaining aspect of the book for me was that the review copy I received had been produced with its cover on upside down and back to front!

Robert I. Cohen, *Consultant Psychiatrist in Adult Mental Illness, Hillingdon Hospital, Uxbridge, Middlesex*

Reconstructing Schizophrenia. Edited by Richard P. Bentall. London: Routledge. 1990. 308 pp. £35.00.

After 100 years of research, the nature of schizophrenia remains as mysterious as ever. Since Bentall's preface promises a new approach to the problem, jaded students of schizophrenia will take up this book with hope. They will be disappointed. There is an echo of the swashbuckling '60s suggestion that schizophrenia is a myth used by wicked psychiatrists to control social undesirables (Marshall, Pilgrim). The echo is faint, because, after 'rigorous scrutiny', most of the contributors agree that there is a genetic basis for the disorder and that there is a place for the use of neuroleptic drugs. Given this admission, attacks on the biological approach to schizophrenia lose much of their force. Rather than saying that there is no biological basis for schizophrenia, the argument is that the biological approach has been exaggerated and that other factors have not been sufficiently examined. Schizophrenia research, they complain, has been too much dominated by psychiatry and the 'medical model'.

Many contributors seem to believe that accepting a biological basis implies that only biological treatments are useful. This is obviously not the case. Barham & Hayward, and Slade & Tarrier show how social and psychological factors can be used to help schizophrenic patients. Of course, this does not reveal anything about the relevance of these factors to the fundamental nature of the disorder. Slade gets closer to fundamentals by relating his approaches to treatment to speculations about the cognitive basis of various symptoms. Ironically, he uses for this purpose the impeccably psychiatric framework developed by Peter Liddle.

The other critique presented in this book concerns the existence of the syndrome 'schizophrenia'. Boyle, Jackson & Bentall argue that the evidence for a unitary syndrome is very weak. Few would disagree with this. New diagnostic schemes and new subgroupings are continually being proposed and many psychiatrists are currently questioning Kraepelin's original formulation. The arguments will continue until the aetiology is fully unravelled. As an alternative to discrete syndromes, Venables & Claridge propose a dimensional approach. Bentall proposes that psychological mechanisms should be sought that relate to specific symptoms, rather than to 'schizophrenia', and presents some of his own work in this direction.

This book brings together critiques of, and approaches to, research on schizophrenia which have appeared before and are not going to cause a revolution. The student of schizophrenia will continue to feel jaded.

Chris Frith, *MRC Scientist, Research Centre, Harrow*

Art Therapy in Practice. Edited by Marian Liebermann. London: Jessica Kingsley Publishers. 1990. 191 pp. £24.50 (hb), £9.95 (pb).

The contributors to this volume all work in the same geographical region and between them cover a wide variety of client groups; acute and long-term psychiatric patients, psychogeriatric patients, people with psychiatric problems with learning difficulties, children with psychological problems, offenders in the community and homeless people.

The variety of their clients is matched by the variety of ways in which they interpret the practice of art therapy. One could almost say that the methodology can stretch from therapy in which art forms the focus of the relationship either with the therapist or the group, to that in which the art itself becomes the therapy which is best left without the intervention of the therapist.

The most important message which is conveyed in this excellent collection lies in its demonstration of the way in which the art therapists have managed to extend their skills in the service of such a wide variety of human distress. It demonstrates the adventurous nature of art therapy which has refused to enclose itself into a rigid pattern of practice but has demonstrated the way in which it can be of value in the most unexpected situations.

It heralds a call to all art therapists to continue to accept any challenge while at the same time may help others to consider its possibilities in fields where, up to now, it has not figured.

LOUIS MARTEAU, *Psychotherapist, Dympna Centre, London*

MMPI–2 Assessing Personality and Psychotherapy. By JOHN R. GRAHAM. Oxford: Oxford University Press. 1990. 335 pp. £27.50.

MMPI–2 in Psychological Treatment. By JAMES BUTCHER. Oxford: Oxford University Press. 1990. 195 pp. £16.00.

The original Minnesota Multiphasic Personality Inventory (MMPI), claimed by both authors of these books to be the most widely used personality inventory, was first published more than 50 years ago. Over these years there have been a number of criticisms concerning the low reliability of the scales, their factorial structure, the fact that many of the items were out of date and the lack of any theoretical underpinning.

The MMPI-2 was developed to overcome some of these problems. These two books describe how this was done and discuss how the new test is to be used in clinical practice. Both authors are acknowledged as experts with the MMPI and were involved with the development of the new version. As might be expected, both books are authoritative. Together they provide all the information necessary to use the MMPI-2.

The new test differs from the old in the following ways. The standardisation sample is far larger and more representative. There can be no doubt that, in this respect, the new test is superior. Items were changed where necessary to improve their relevance, and new ones were written to extend the scope of the test. Some items which had proven objectionable were removed. This modified item pool was tried out and the best items were selected for the scales. Both authors insist that these modifications improve the test, but allow the new scales to be interpreted in the light of the vast research on the old form.

The items of the new scales certainly appear to be an improvement, although the internal consistency of the scales is still low. Only five have alphas above 0.7 and this is still far too low to be confident of the test scores. Similarly, the evidence for the validity of the new scales is far from convincing. For example, rating scales are used as a criterion for the scales' scores. However, the correlations reported are very low; the sample size was so huge that a non-significant correlation must have been hard to obtain. Furthermore, rating scales are somewhat similar to the items so that some overlap is inevitable.

These books are complementary rather than competitive. That by Graham gives all the information about the test which a user is likely to need and it serves as a useful reference book. That by Butcher is more specialised, being concerned with the use of the MMPI-2 as a guide for treatment. However, although shorter, it contains a good description of MMPI-2.

In summary these are sound, authoritative books on the new MMPI-2. They are essential reading for anyone who intends to use the test. My disappointment with both of these books is that they are too uncritical, although I suppose that this is inevitable, given the involvement of their authors with the test.

PAUL KLINE, *Professor of Psychometrics, University of Exeter*

The Preschool Child: Assessment, Diagnosis and Treatment. By PAUL V. TRAD. Chichester: John Wiley & Sons. 1989. 658 pp. £50.75.

This book sets out to provide an "integrated approach to the developmental phenomena that occur in children of preschool age" (2–6 years). It has five sections: the developmental perspective, assessment, clinical syndromes, specific risk factors during the preschool years, and management.

The orientation of the book is clearly North American, with the use of DSM–III–R terminology throughout. The text is liberally supported by references, including recently published work, and enlivened by case illustrations.

It is certainly comprehensive, covering not only a wide range of issues, but a wide range of childhood psychiatric conditions and approaches to treatment. As far as specific conditions are concerned, the author does not confine himself to those which occur only in the preschool child, and in discussing these conditions the book resembles a general textbook of child psychiatry. Nevertheless, a great deal of emphasis is placed on the developmental issues particularly associated with preschool children, with great emphasis on the role of play in both assessment and management. The author is clearly dynamically orientated in his approach to therapy, and the sections on behaviour therapy in particular do not do justice to the extent to which these methods are applicable to preschool problems.

Many British child psychiatrists will find some sections startling – for example, that on personality disorders in preschool children. Little attention is paid to prevention of problems in this age group.

This book is a valuable contribution to the currently available texts on child psychiatry as it succeeds in addressing many of the specific issues concerned with the assessment and management of preschool children with psychiatric problems.

GILLIAN FORREST, *Consultant Child Psychiatrist, The Park Hospital for Children, Oxford*

Children of Battered Women. By Peter G. Jaffe, David A. Wolfe and Susan Kaye Wilson. London: Sage Publications. 1990. 132 pp. £10.95.

This little book is the latest in a series from the publisher which brings together information on specific aspects of child psychiatry, which might otherwise be scattered through a range of publications for different professionals. In this wide area of children involved in domestic violence this means that developmental child psychology, child psychiatric symptoms, sociological data and the law can be brought together to develop a rationale for intervention and treatment in a coherent framework. This is not just informative and helpful for focusing on the problem but also gets around the false dichotomy which sometimes arises in topics like this between 'real psychiatry' and 'social problems'.

The material is logically organised. Chapter 1 gives an overview of domestic violence, although only from North America. Chapter 2 reports on specific studies on children in refuges, using a developmental perspective to understand the different responses that children can display. Chapter 3 looks at theoretical aspects of the link between domestic violence and future problems in the children and the fourth chapter draws this together in a logical framework for assessment and treatment at primary, secondary and tertiary levels. The last chapter is possibly the least directly helpful, as it looks at the implications for various agencies if they take the needs of this group of children seriously. Again, it discusses the North American structure, although there are some similarities.

This is not a book which develops new theories, but it usefully organises theoretical aspects around clinical findings in children who, as part of the spectrum of victims and survivors of abuse, form a significant part of clinical practice but often an insignificant part of standard textbooks. Adult mental health workers would find it equally useful as a reminder of the importance of this problem and its relevance to psychological functioning.

Rachel Leheup, *Consultant Child and Adolescent Psychiatrist, Nottingham*

Human Aggression: Naturalistic Approaches. Edited by John Archer and Kevin Browne. London: Routledge. 1989. 284 pp. £35.00 (hb), £12.95 (pb).

The editors suggest that the naturalistic approach to the study of aggression offers the best basis for identifying, preventing and treating violent behaviour. Given that the naturalistic approach eschews the laboratory in favour of viewing aggression in the context of the interactions, relationships and situations in which it occurs, that might seem a statement of the obvious. What is less easy to accept is the assertion that human aggression is one of the most pervasive and serious problems facing modern societies. What are the others? Put another way, the editors claim to have identified in aggression one of the major issues for modern mankind. By following their approach you stand the best chances of preventing and treating violent behaviour. This is too good to miss!

With that promise it is not surprising that the book is disappointing. The eleven psychologists who have contributed to this well edited and cohesive volume all adopt a common-sense approach to the subject which left this reader with the impression that he had not learned anything new. The book's weakness lies in an absence of almost any reference to the psychopathology and phenomenology. Its strengths are in Beynon's chapter, "A school for men: an ethnographic case study of routine violence in schooling", and Howells' chapter "Anger management methods in relation to the prevention of violent behaviour".

Surely psychiatrists, like general practice receptionists, would benefit greatly from a proficiency in anger management?

Paul Bowden, *Maudsley Hospital, London*

Psychology in Prisons. By David J. Cooke, Pamela J. Baldwin and Jacqueline Howison. London & New York: Routledge. 1990. 147 pp. £25.00.

This book aims to give a deeper understanding of why offenders sometimes behave in unusual and unexpected ways when held in custody. The main emphasis of this book is to explain how a knowledge of psychology would improve prison officers' ability to deal with offenders. The book argues that by applying psychological principles, behaviour within prisons can be better understood and violence and stress can be limited.

The three authors are all psychologists who have worked extensively with prisoners and prison staff. Their book is divided in two sections; the first section is concerned with the origins of criminal behaviour, while the second half of the book attempts to show how psychology can be applied to be more effective in the day-to-day job of dealing with prisoners.

The 13 chapters deal with virtually the whole range of crime. The chapter on understanding violence and aggression is of particular interest. Chapters on coping with disturbed prisoners and facing violence will be of direct relevance to most staff working in prisons.

Highly topical are the chapters on the impact of AIDS in prison life, and hostage-taking in prison.

The book is primarily geared towards prison officers; this will somewhat limit the interest of mental health professionals working, for example, in the field of forensic psychiatry. Further limitations are a non-existing list of references and a rather limited two-page index. The price for the hardback appears rather steep; a possibly less expensive paperback version is not available.

The book will probably not find its way into the recommended reading list of psychiatrists or other mental health professionals working in the forensic field. Nevertheless it might have its place in the field this book is intended for: training and helping prison officers to understand the behaviour of prisoners and to help them to deal with the aggression, the distress and the difficulties of the prisoners in their charge.

HEINZ ALBRECHT, *Specialist Psychiatrist, Regional Forensic Services, Auckland Area Health Board, New Zealand*

Epidemiology and the Prevention of Mental Disorders. Edited by BRIAN COOPER and THOMAS HELGASON. London: Routledge. 1989. 367 pp. £40.00.

This is a compilation of reports and review articles presented at the ninth scientific symposium of the World Psychiatric Association's Section of Epidemiology and Community Psychiatry. The theme is prevention in psychiatry. The editors suggest that a cursory glance through the best known American and British textbooks suffices to show that "prevention remains today a grossly undervalued theme" in psychiatry. Sartorius, in his summary of the World Health Organization's view on prevention concurs – "work in the field of mental health is not seen as a public health effort and mental diseases are not considered a public health problem". In compiling these papers the editors are attempting to redress the balance with, as they put it, a "small but significant landmark in the development of psychiatric epidemiology as a public health discipline". How far do they succeed?

At first glance this book creates a 'heart-sink feeling' similar to that produced by some patients. There appears a disparate collection of articles, ranging from "the sociodemographic risk factors of depression in octogenarians" to "multilevel approaches to the prevention of mental disorders in the community: the Athenian experience". On the face of things, just another collection of loosely related topics gathering together data, much of which has been published elsewhere.

A closer inspection shows this to be a quite misleading impression. The editors must be congratulated on their skilful organisation of the material in line with their overall objectives. The introduction by Cooper gives a superb overview of the issues related to prevention in psychiatry; naive and grandiose designs for "transforming the health of the community" are firmly discarded, while the reader's enthusiasm is kindled for goals that are both realistic and attainable. The book is worth looking into for the introduction alone.

A series of papers are organised into six sections, each dealing with some aspect of prevention. Inevitably, given the variety of authors, the material varies considerably in both style and quality. The editors have selected presentations of a generally high standard, however, and the chapters on vulnerability, the epidemiology of Alzheimer's disease and unravelling the causes of homelessness are notable.

Most readers will not wish to attempt to assimilate detailed data on so many widely differing subjects. This is perhaps a book to be dipped into rather than read from cover to cover. Nevertheless, the editors have probably succeeded in their ambition – this is a small but significant landmark in thinking about strategies for prevention in psychiatry.

GLYNN HARRISON, *Consultant Psychiatrist, Department of Psychiatry, University Hospital, Nottingham*

Clinical Pharmacology of Psychotherapeutic Drugs. (3rd edn). By LEO E. HOLLISTER and JOHN G. CSERNANSKY. London: Churchill Livingstone. 1990. 194 pp. £27.00.

The previous edition of this book appeared in 1983 and clearly it was due for a revision, given the changes in psychopharmacology over this time. The book is written jointly by the authors, thereby avoiding the problems of multiple authorship. It succeeds in its aim to provide a brief, readable and useful reference to the main groups of psychotropic drugs. The main problem for readers on this side of the Atlantic is that it is written from an American perspective with emphasis on DSM–III disorders, and the literature cited is predominantly from US sources. UK readers will find some differences in prescribing habits, for example, in the use of benzodiazepines, and will be frustrated that a number of drugs are not described because they are not available in the USA.

The book is divided into seven chapters, including a new chapter on the drug treatment of childhood disorders. Each chapter begins with a brief history of the drugs in question, followed by a discussion of the relevant disorders, their epidemiology, nosology and aetiology, and how our understanding of these disorders relates to psychopharmacology. The different types of old and new drugs are considered, in terms of their structure, pharmacokinetics, mode of action, dosages and dosage schedules, treatment duration, side-effects, effects of overdose, drug interactions and consideration of their uses clinically.

The first chapter provides a general overview. The second chapter on antianxiety drugs encompasses newer drugs, such as those acting on 5-hydroxytryptamine (5-HT) receptors. Although reasonable guidelines are provided for the prescription of benzodiazepines, they are viewed with less circumspection than in the UK and are considered appropriate in a number of disorders, including alcohol withdrawal, mild depression and schizophrenia. Chapter three deals with the pharmacotherapy of sleep disorders, although narcolepsy is not mentioned until the final chapter. The next chapter on antidepressants provides a very useful review, but UK drugs such as mianserin are not included. Some newer drugs, for example, the 5-HT reuptake inhibitors and the specific MAO-A (monoamine oxidase-A) and MAO-B inhibitors are described. There is a useful section on plasma monitoring and the issue of combination therapy is discussed, with words of caution about combining 5-HT reuptake inhibitors with other drugs. Chapter five deals with the psychoses and covers key issues, such as low-dose scheduling, treatment resistance and combination therapy. The discussion on clozapine is of interest as it has only recently been marketed in the UK. On the other hand pimozide is not used in the US and is consequently not mentioned, and haloperidol is the only butyrophenone used for psychosis. The role of long-acting depot medication is considered controversial in the majority of patients, although the evidence cited is selective. The section on adverse drug reactions, including movement disorders and the neuroleptic malignant syndrome, is useful. The latter are discussed at length in this short book, probably reflecting the greater concern over issues of litigation in the USA. Chapter six deals with mood-stabilising drugs and is particularly informative on the use of lithium and carbamazepine. The final chapter is on the drug treatment of disorders of childhood and adolescence. It focuses on 'attention-deficit' disorder and autism, with brief mention of other conditions, including a section on mental retardation.

This is a useful reference book, with a clear layout and readable style, providing up-to-date information on questions of the psychopharmacology of a number of psychiatric drugs. The major limitation of this book is that it is written for the psychiatrist in the USA. This, together with the price, is likely to make it less attractive to readers in the UK.

CHRISTOS PANTELIS, *Lecturer in Psychiatry,*
Charing Cross & Westminster Medical School,
Academic Unit, Horton Hospital, Epsom, Surrey

The Essential Guide to Psychiatric Drugs. By JACK GORMAN. New York: St Martin's Press. 1990. 397 pp. $22.95.

This book is concerned with the nature, actions, uses and side-effects of psychotropic drugs in current use. Equally important is the full attention given to the patient's needs and setting. The descriptive section is preceded by several chapters in which psychopharmacology and the two main approaches in psychiatric treatment are described. Advice is given on how to decide if you need a psychotropic compound, the points to consider before seeing a psychiatrist, and the basis on which to choose your prescriber. An explanation of side-effects and discussion on length of treatment conclude the detailed introduction.

In the 250 pages of the reference guide, drugs are classified according to their clinical function and the headings refer to treatment of depression, anxiety, bipolar affective disorder and schizophrenia. Drugs for insomnia and for the treatment of drug abuse are well covered. In each section, when appropriate, there is a guide to when treatment is necessary, a classification of the disorder, a list of symptoms, ways of reaching a diagnosis (DSM–III–R is used) and a comparative review of the drugs available. Each drug is then described individually.

The later chapters cover the treatment of violence, weight loss and gain, pregnancy, treating the problems of AIDS, genetic links, brand names and 'how psychiatric drugs work'. There is a short glossary. Throughout, the author looks realistically at patients' (and relatives') needs, pulling no punches about how to ensure satisfaction. In doing so he conveys something of the scene of psychiatric practice in the United States. An estimate of the level of sophistication and recency may be gained from the inclusion of amoxapine, fluoxetine and carbamazepine but no mention of thyroid.

Bearing in mind it is written for the US public, it can be recommended to patients without reservation. Perhaps it also provides (unwittingly) the psychiatrist with an interesting source of self-audit inexplicably difficult to locate in our professional textbooks.

JOHN POLLITT, *Honorary Consulting Physician in*
Psychological Medicine, St Thomas' Hospital,
London

Bizarre Behaviours. By HERSCHEL PRINS. London & New York: Tavistock/Routledge. 1990. 111 pp. £25.00 (hb), £9.99 (pb).

Prins is perhaps best known for his hunt for vampires; a search which seems now to have preoccupied him for a number of years. This is the focal part of his book and constitutes its principal and longest chapter. How successful has his hunt been?

There is plenty of mythology and folklore here, but precious little hard fact. A circular questionnaire sent to 45 persons (34 of them psychiatrists – I think I remember being one of them) who might possibly have been expected to have had some first-hand knowledge of this esoteric condition, seems to have produced no actual cases. While the survey of the literature is extensive, not only of vampirism, but of other engaging mysteries, its main weakness is the inability of its author to draw upon his own first-hand experiences.

Apart from vampirism, Prins deals with a number of other somewhat obscure psychiatric conditions, some of them exotic and oriental; some nearer home. Again, while the review of the literature on these topics is of considerable value, accounts couched in terms of first-hand experience are, once again, conspicuously lacking.

In writing about so-called 'culture-bound syndromes' – Amok, Koro, Susto, Latah and others – Prins makes the interesting point (which I must say had previously escaped me) that nearer home, we also have our own such syndromes e.g. overdoses, agoraphobia, some forms of shoplifting and baby-snatching. He could also perhaps have added anorexia nervosa to the list, as this seems to be a rare condition further afield.

While this is a book which might not be of too much help to those aspiring towards the MRCPsych, it is certainly a good read! Thus, although the eponym Kotzwarra's syndrome was new to me, the condition it describes is not, unfortunately, too rare or altogether unfamiliar. But to find out to what it refers you may need to buy a copy of the book. It could well turn out to be worthwhile.

W. H. TRETHOWAN *Emeritus Professor of Psychiatry, University of Birmingham*

Quantitative Data Analysis for Social Scientists. By ALAN BRYMAN and DUNCAN CRAMER. London: Routledge. 1990. 290 pp. £10.95.

This is an attractive and well laid-out book, which primarily covers the topics usually dealt with in an introductory course in statistics, such as the summarisation of data, inference, and correlation. Additionally, however, the authors have chosen to include three more advanced chapters which cover analysis of variance and factor analysis.

A particular feature of the text is its replacements of formulae of the mathematical variety, with codes for SPSS programs. In general I do not find a mixture of textbook and programming manual appealing, but here the authors have managed to combine the two very successfully. Many data sets are provided and the exercises at the end of each chapter should prove very helpful to students.

Overall then a useful addition to the introductory statistics text market, although the authors themselves might prefer 'introductory quantitative data analysis.'

BRIAN EVERITT, *Professor, Institute of Psychiatry, London*

The Clinical Relevance of Kindling. Edited by TOM G. BOLWIG and MICHAEL R. TRIMBLE. Chichester: John Wiley & Sons. 1989. 302 pp. £40.00.

When Graham Goddard first described the development of epileptic seizures through brain stimulation at low intensity one wonders whether he had any insight into the amount of work and speculation his findings would provoke. One suspects he would have been surprised that more than 20 years later a volume would appear to discuss the relevance of 'kindling', not only to human epileptogenesis but also to memory formation, anxiety, alcohol and cocaine withdrawal, epileptic psychosis, manic-depressive psychosis, panic attacks and tardive dyskinesia. He would no doubt have been disappointed that the clinical relevance of kindling, even to human epilepsy, remains uncertain and that no clear clinical advances have resulted from the understanding of the neuronal processes involved in kindling and epileptogenesis in the laboratory animal.

This is a multi-authored edition from the proceedings of a symposium sponsored by Ciba-Geigy. For those unfamiliar with the field the early chapters are most useful as they deal with the mechanisms and current state of knowledge of both electrical and chemical kindling and the effects of antiepileptic drugs on this phenomenon. Subsequent chapters deal with further evidence that might possibly link kindling or kindling-like phenomena to other clinical areas.

The chapters are linked together into related groups which are followed by accounts of the discussion that took place in the workshops. The most revealing discussion is the final one, which attempts to bring a hard definition to the phenomenon. Up to this point the reviewer, a neurologist, had become more and more confused as to precisely what could and could not be encompassed by the kindling phenomenon. The discussion brings the reader back to reality with a painful bang. Kindling is in essence a non-physiological stimulus that can result in seizures in experimental animals. Taking the concept beyond the specific into the more general areas explored by this book has to be a questionable process, particularly where the clinical syndromes to which the hypothesis is applied are ones that are poorly defined and may well be heterogeneous in their make-up. Perhaps this book is as much a monument to clinicians' enthusiastic adoption of possibly over-simple hypotheses to explain clinical phenomena in their own fields, as much as to kindling itself.

There is no doubt that while the book contains chapters of widely differing merit it is a useful state-of-the-art summary for anyone wishing to read about the subject. To the outsider it appears very introspective and the workshop and the book might have benefited from the presence of critical outsiders producing more clinically relevant discussion. As is often the case with chapters written as a result of a symposium, many contain little in the way of original information and are available in only slightly different forms in other publications. For the average clinical psychiatrist or neurologist the book will make an informative and stimulating read, but one wonders whether there should not be some form of 'health warning' to go with the more speculative aspects of this publication.

DAVID CHADWICK, *Consultant Neurologist, Walton Hospital, Rice Lane, Liverpool*

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Contents of *The American Journal of Psychiatry*

March 1991 Volume 148

Special Articles

Genetics and psychiatry: an unheralded window on the environment. *David Reiss, Robert Plomin and E. Mavis Hetherington* 283
Substance abuse and cerebral blood flow. *Roy J. Mathew and William H. Wilson* 292
Self-injurious behavior: a review of the behavior and biology of self-mutilation. *Ronald M. Winchel and Michael Stanley* 306

Regular Articles

A psychodynamic perspective on the clinical impact of insurance review. *Glen O. Gabbard, Tetsuro Takahashi, Joyce Davidson, Marceil Bauman-Bork and Kenneth Ensroth* 318
Psychological comorbidity and length of stay in the general hospital. *Stephen M. Saravay, Maurice D. Steinberg, Barbara Weinschel, Simcha Pollack and Nancy Alovis* 324
Housing instability and homelessness among rural schizophrenic patients. *Robert E. Drake, Michael A. Wallach, Gregory B. Teague, Daniel H. Freeman, Thomas S. Paskus and Timothy A. Clark* 330
A critical appraisal of mitogen-induced lymphocyte proliferation in depressed patients. *Denis F. Darko, Nevin W. Wilson, J. Christian Gillin and Shahrokh Golshan* 337
12-month outcome of patients with major depression and comorbid psychiatric or medical illness (compound depression). *Gabor I. Keitner, Christine E. Ryan, Ivan W. Miller, Robert Kohn and Nathan B. Epstein* 345
Depressive symptoms following stroke. *Robert A. Stern and David L. Bachman* 351
The nature and course of olfactory deficits in Alzheimer's disease. *Michael Serby, Pamela Larson and Davina Kalkstein* 357
Nonfearful panic disorder in neurology patients validated by lactate challenge. *Johnna L. Russell, Matt G. Kushner, Bernard D. Beitman and Kim M. Bartels* 361
Characteristics of 60 adult chronic hair pullers. *Gary A. Christenson, Thomas B. Mackenzie and James E. Mitchell* 365

Clinical and Research Reports

Nortriptyline treatment of depressed cardiac transplant recipients. *Peter A. Shapiro* 371
Transdermal nicotine and smoking behavior in psychiatric patients. *Neil Hartman, Gregory B. Leong, Shirley M. Glynn, Jeffery N. Wilkins and Murray E. Jarvik* 374

Contents of *The Journal of Nervous and Mental Disease*

March 1991 Volume 179

Patterns of neuropsychological impairment after severe blunt head injury. *R. L. Tate, B. Fenelon, M. L. Manning and M. Hunter* 117

Neuropsychological performance in patients with mild multiple sclerosis. *Harry Klonoff, Campbell Clark, Joe Oger, Don Paty and David Li* 127

Optical differences in multiple personality disorder: a second look. *Scott D. Miller, Terrell Blackburn, Gary Scholes, George L. White and Nick Mamalis* 132

Psychiatric symptoms in mentally ill chemical abusers. *Michael P. Carey, Kate B. Carey and Andrew W. Meisler* 136

Gender roles, social support, and postpartum depressive symptomatology: the benefits of caring. *Judith A. Richman, Valerie Raskin and Cheryl Gaines* 139

Dependency and eating disorders in female psychiatric inpatients. *Robert F. Bornstein and Roger P. Greenberg* 148

Borderline personality disorder in young Swedish suicides. *Bo Runeson and Jan Beskow* 153

Self ratings of anger and hostility in borderline personality disorder. *David L. Gardner, Ellen Leibenluft, Kathleen M. O'Leary and Rex W. Cowdry* 157

The impact of a humanmade disaster on the utilization pattern of a psychiatric emergency service. *David A. Fishbain, Tim E. Aldrich, Myron Goldberg and Robert C. Duncan* 162

Demoralization and social supports among Holocaust survivors. *Shmuel Fenig and Itzhak Levav* 167

Brief Reports

Lysergic acid diethylamide-induced chronic visual disturbances in an adolescent 173

Episodic alcoholism 174

Books. Andreasen, N. C. (ed.) *Schizophrenia: Positive and Negative Symptoms and Syndromes*; Fleagle, J. G. *Primate Adaptation and Evolution*; Eib-Eibesfeldt, I. *Human Ethology*; Rasa, A. E., Vogel, C. and Voland, E. (eds) *The Socio-Biology of Sexual and Reproductive Strategies*; Miller, A. H. (ed.) *Depressive Disorders and Immunity*; Horowitz, M. J. *Introduction to Psychodynamics: A New Synthesis*; Albert M. S. and Moss, Mark B. (eds) *Geriatric Neuropsychology*; Winett, R. A., King, A. C. and Altman, D. G. *Health Psychology and Public Health: An Integrative Approach* 175

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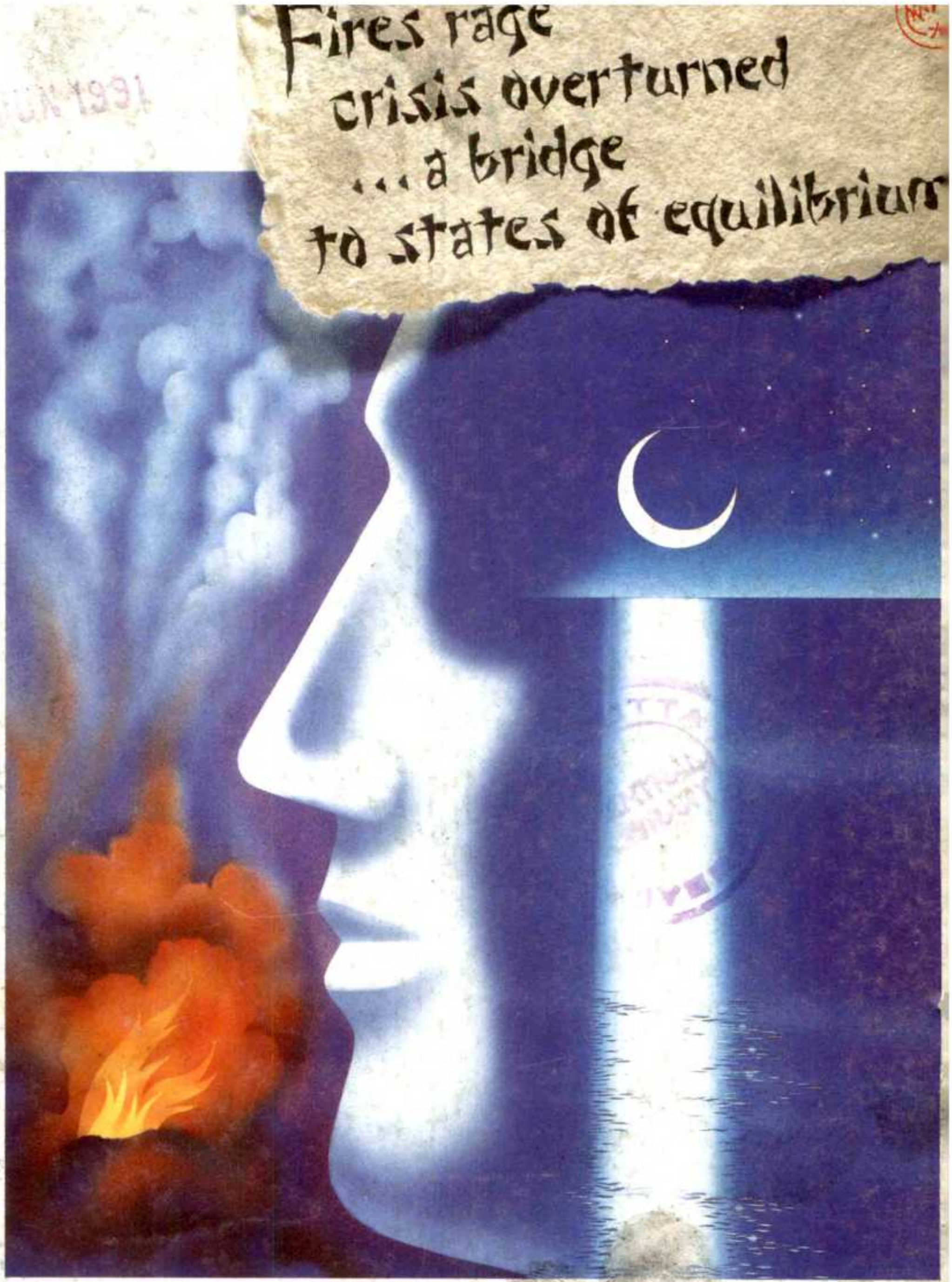

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May 1991 Vol. 158

Lecture

Jealousy: the pathology of passion. *P. E. Mullen* 593

Molecular Biology Symposium

Molecular genetics of the major psychoses: the role of the Medical Research Council. *D. A. Rees and K. Levy* 602

Collaborative strategies in the molecular genetics of the major psychoses. *M. Leboyer and P. McGuffin* 605

The search for the psychosis gene. *T. J. Crow* 611

The genetics of schizophrenia is the genetics of neurodevelopment. *P. Jones and R. M. Murray* 615

Papers

Evidence for a pseudo-autosomal locus for schizophrenia using the method of affected sibling pairs. *J. Collinge, L. E. DeLisi, A. Boccio, E. C. Johnstone, A. Lane, C. Larkin, M. Leach, R. Lofthouse, F. Owen, M. Poulter, T. Shah, C. Walsh and T. J. Crow* 624

No genetic linkage detected for schizophrenia to Xq27–q28. *L. E. DeLisi, T. J. Crow, K. E. Davies, J. D. Terwilliger, J. Ott, R. Ram, T. Flint and A. Boccio* 630

No evidence for a susceptibility locus predisposing to manic depression in the region of the dopamine (D2) receptor gene. *D. Holmes, J. Brynjolfsson, P. Brett, D. Curtis, H. Petursson, R. Sherrington and H. Gurling* 635

Changes in patient coping style following individual and family treatment for schizophrenia. *M. M. Rea, A. M. Strachan, M. J. Goldstein, I. Falloon and S. Hwang* 642

Negative modes of relating, marital quality and depression. *J. Birtchnell* 648

Plasma levels of fluphenazine in patients receiving fluphenazine decanoate. Relationship to clinical response. *S. R. Marder, K. K. Midha, T. Van Putten, M. Aravagiri, E. M. Hawes, J. W. Hubbard, G. McKay and J. Mintz* 658

Lithium treatment and prophylaxis in unipolar depression: a meta-analysis. *F. G. M. Souza and G. M. Goodwin* 666

Social influences on the course of anxious and depressive disorders in school-age children. *I. Goodyer, E. Germany, J. Gowrusankur and P. Altham* 676

Care of chronic neurotic out-patients by community psychiatric nurses. A long-term follow-up study. *T. Burns, E. S. Paykel, A. Ezekiel and S. Lemon* 685

Facial dyskinesia: a 16-year follow-up study. *H. A. McClelland, A. V. Metcalfe, T. A. Kerr, D. Dutta and P. Watson* 691

A comparison of the withdrawal responses of heroin and methadone addicts during detoxification. *M. Gossop and J. Strang* 697

Continued inside

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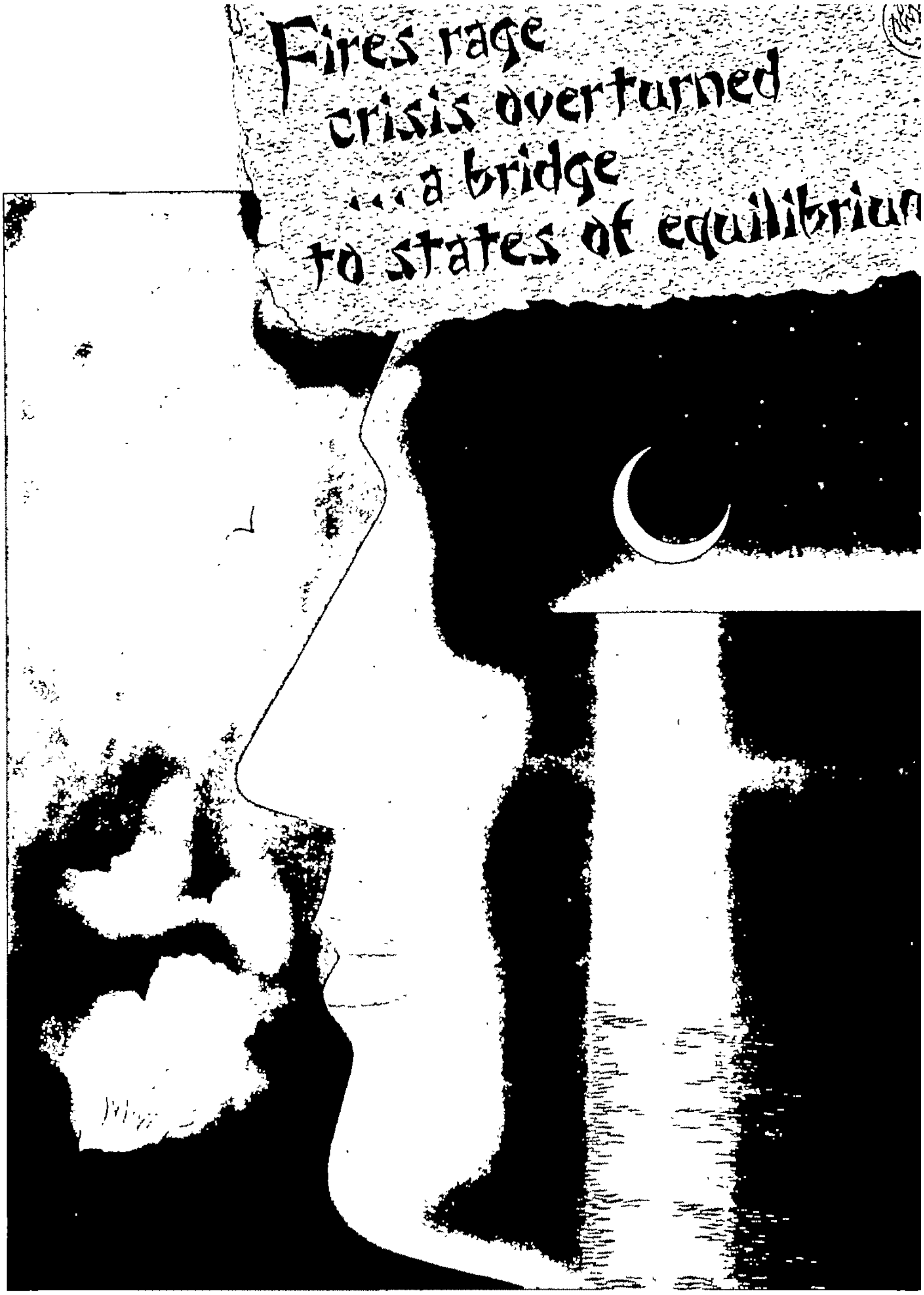

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Contents continued from front cover

Interictal psychopathology in epilepsy. Prevalence and pattern in a Nigerian clinic. *O. Gureje* 700

Point of View

The myth of elevated serum creatine phosphokinase level and neuroleptic malignant syndrome. *Adityanjee* 706

The Current Literature

Is sex necessarily a risk factor to depression? *T. Harris, P. Surtees and J. Bancroft* 708

Columns

Correspondence 713
A hundred years ago. *Researched by H. Rollin* 722
Reading about... Group psychotherapy. *M. Hobbs* 723
Book reviews 726
American Journal of Psychiatry (contents) 736
The Journal of Nervous and Mental Disease (contents) *facing* 736

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Lecture

Jealousy: The Pathology of Passion

PAUL E. MULLEN

Emotions may be rooted in biology but the process of cultural construction gives those emotions form and a language for their expression. The changing construction of jealousy in Western societies has transformed a socially sanctioned response to infidelity into a form of personal pathology which is the mere outward expression of immaturity, possessiveness and insecurity. This is a history of the stripping away of social, ethical and finally interpersonal meanings from an experience, to leave it as a piece of individual psychopathology. Fidelity and jealousy are constructed as they are because of the nature of the social and economic realities which drive our culture. The erosion of the area of human experience which could be identified with normal jealousy leaves the boundary between the pathological jealousy of psychiatry and normal experience increasingly problematic.

Jealousy can confront the psychiatrist in a variety of guises. Convictions about the partner's infidelities may form the content of psychopathological phenomena such as delusions (Jaspers, 1910; Lagache, 1947; Shepherd, 1961; Mullen, 1990*a*). When jealousy arises not as a symptom of obvious underlying disorder, but as a reaction to some understandable threat to the relationship, then the distinction between the responses of those 'normally' and those 'pathologically' jealous can present formidable problems (Vaukhonen, 1968; Retterstol, 1967; Tiggelaar, 1956; White & Mullen, 1989). These problems are compounded by the absence of any clear notion of what constitutes normal jealousy and where the boundaries of that normality, in terms of both behaviour and experience, should be drawn. It is accepted that jealousy is a common, if not universal, experience, but despite this, its status as 'normal' is in increasing doubt.

Eliot Slater argued that psychiatrists could, and should, apply their particular perspective to issues of social and cultural importance to contribute to the common pool of understanding. This paper examines jealousy as a construct which is altering with the changing cultural contingencies of Western societies in the hope of shedding some light on why normal jealousy has become problematic.

The manner in which jealousy is regarded and experienced has changed repeatedly over the history of Western societies. The changing cultural construction of jealousy has gradually transformed it from a socially sanctioned response to infidelity into a personal pathology. In the 17th century jealousy was a passion, albeit one that could cause problems. Today jealousy is a problem which can stir up damaging and embarrassing emotion. Jealousy was once a passion which had a role in expressing and maintaining individual and social values which, admittedly, if uncontrolled could usher in pathology. Today jealousy is often regarded as a pathology which offends against the ethics of liberal individualism and its free market in goods, ideas and people. Jealousy is riven by contradictions. At one extreme it embodies a longing for an ideal in human relationships and a cry of protest at the loss of that dream of sustained commitment and fidelity. At the other, it has always been contaminated by the attempt to impose the desires and priorities of one person upon another. The changing balance between destructive possessiveness and disappointed hope is central to jealousy's history. The path that jealousy has travelled from the zealousness of the Renaissance to become a hallmark of personal immaturity is examined here in terms of the changing construction of emotion and the alterations in patterns of sexual behaviour.

There are a number of assumptions implicit in interpreting emotions as being in part cultural construction. One is that we are subject to a multiplicity of emotions and desires but we only have names for some of them and, by and large, only the grosser examples. Jealousy, as a self-description, covers a wide range of potential experiences, a range which alters according to the constructions of the individual and the wider culture. In speaking of emotions and desires we are limited by the language of our culture and perforce we fit our experiences as best we can into the available vocabulary. Over time this vocabulary changes. Finlay-Jones (1983)

This paper is based on the 1990 Eliot Slater Memorial Lecture.

described the disappearance of the emotion *accidie* from Western culture, but more importantly, claimed that a group of those who now call themselves depressed, would have found better expression for their state of mind within the lost language of *accidie*. The relationship between experience and the words used to express that experience is a two-way process and in our culture of prefabricated feelings, words and phrases increasingly give birth to reality (Adorno, 1973). To begin to know about a person's emotions and desires it is necessary to embark on an archaeology both of their own personal development and their culture's words.

The changing face of jealousy can be introduced by looking at some of the virtues and vices attributed to jealousy in different historical periods. The word 'jealousy' carried with it in the 14th century the connotation of eagerness, devotion and zealousness (*Oxford English Dictionary*, 1971). It implied a solicitousness to preserve something possessed or esteemed. The adage attributed to St Augustine that who is not jealous does not love ("Qui non zealat non amat") surely speaks more to the enthusiasm of love than to possessiveness or suspicion. The potential for any solicitousness and devotion in jealousy to give way to suspicion and distrust has long been recognised. Thus in *Othello* (1694) Shakespeare has Emilia tell Desdemona: "They are not ever jealous for the cause, but jealous for they're jealous. Tis a monster begot upon itself, born on itself".

Jealousy, despite its attendant darker side, was accorded a role in preserving social esteem in societies ruled principally by concepts of honour. Honour, at least as an ideal, involves an uncompromising pursuit of the good which puts aside individual advantage in preference to moral and social principle. Where monogamy is a moral and social imperative, jealousy is regarded as a protector of the integrity of the family. Gonzales-Crussi (1988), in an essay on male jealousy, which harks back nostalgically to a Spanish culture still ruled by codes of honour, claimed the modern era "turns a sanctimonious eye" on jealousy, seeing it as "but a sign of sociopathic or psychological maladjustment" and fails to credit that "jealousy is not without worthy elements" for it "stems at bottom from a concern for the inviolate perfection of others". The balance between the perceived virtues and vices of jealousy has shifted at different historical periods to culminate in the modern view of jealousy as compounded of vices mitigated by little, if any, virtue. Stearns (1989), in his pioneering work on the evolution of jealousy in America, put the position succinctly when he wrote, "for over 60 years all the evaluations of jealousy, scholarly and popular, supportive of, or hostile to, conventional monogamy condemn the emotion". Jealousy is now described as a disaster to be avoided whenever possible (Fisher, 1990). The 'official' view of jealousy does not necessarily reflect the attitudes and practices of those currently living in Western societies, let alone members of different cultures. In a recent survey of jealousy nearly half the respondents agreed with the proposition that jealousy is an inevitable part of love and only a tiny minority disclaimed any experience of the emotion in their sexual relationships (Mullen *et al*, in preparation).

Jealousy survives, if not thrives, in our societies. To understand how it is constructed and experienced at the end of the 20th century it is necessary to briefly examine the conceptualisations of emotions in general. There is a wide range of views on what constitutes an emotion. At one extreme, emotions are regarded as conditioned or unconditioned reactions to stimuli in which reason and judgement have no part. MacNaughton (1989), in his book on the biology of the emotions, coyly disclaimed any desire, or necessity, to define emotion, but finally stated emotions are "in essence any state, or set of states, of the organism which involve the co-occurrence of specific patterns of response of more than one of the skeletal, autonomic and hormonal systems". In such an interpretation the conscious mind is in absence. At the other extreme, the American philosopher Robert Solomon (1980) claimed "emotions are defined primarily by their constitutive judgements, given structure by judgements, distinguished as particular emotions (anger, love, envy etc.) by judgements". Here cognition is all, and biology together with instincts and automatic reactions are nowhere. I do not attempt to resolve the conflict between such formulations but give a passing glance at how two such very different constructions emerged and how they impact on our view of jealousy.

MacIntyre (1988) made elegant use of the Homeric poems and subsequent translations to illustrate the perceived relationship between practical reasoning and emotion at different historical periods. The translators of Homer's epic poems project the traditions and discourse of their own age back onto the Homeric template, thus providing an accessible record of the changing understanding of what constitutes emotion. If we take the example of the passage in the *Iliad* where Achilles is subjected to a public insult from Agamemnon, according to MacIntyre's rendering of Homer he suffers a momentary indecision as the passion of anger infects, or is inflicted on, his 'humus' (spirit, the force which propels the person toward action) before his 'arete' (virtue, duty to fulfil his proper role) reasserts itself. He is helped in this by the prompting of the goddess Athena.

Passion, for Homer, is external and infects the individual, bringing blind infatuation, or in this case, blind rage, but it also has a social and moral dimension. It brings with it the danger of being diverted from the lawful path, from the path of destiny. The concept of passion as external and penetrating is common in early Indo-European societies where emotions are often likened to illnesses which invade or insinuate themselves into us (Crespo, 1986). A surviving image from such emotionologies is that of Cupid firing his dart into the love-struck victim and we still speak of being infected by jealousy. What then of the jealousy of Menelaus confronted by Helen's infidelity. Homer tells us little of his immediate responses, but the whole Trojan War stems from the duty Menelaus accepted to avenge this public humiliation. The infidelity was an insult to his person, to his kingship and to the morality of the society. It placed upon him the duty to avenge the affront and gave him the right to call all Greeks to his assistance. Homer has Helen castigate herself for the adultery as "a whore and a nightmare of a woman" and she attributes the infidelity to "harlotry in me and madness [in Paris] " (Fitzgerald's translation, 1984). This is an infidelity with associated jealousy which can only be understood in terms of moral imperatives, honour and adherence to one's social role.

If we turn to Chapman's translation of Homer from the late 16th century, dominated intellectually as it was by the rediscovery of Aristotle, Achilles is transformed from Homer's publicly humiliated hero infected by anger into a prototype for an Aristotelian debating society, in which, for Chapman, Achilles "at this stood vexed", his heart

> "Bristled in his bosom and two ways did draw his discursive part
> If from his thigh his sharp sword drawn, he should make room about
> Atrides person slaughtering him, or sit his anger out
> And curb his spirit. While these thoughts strived in his blood and mind . . ."

There stands indecisive Achilles immersed in an internal debate about the correct course to follow. Anger is presented as an event separate from the rational mind which can be thoughtfully considered and then acted upon as reason dictates. Passion, emotion as we know it, has almost disappeared, buried under the discursive deliberations of an educated rationality. Cognitions are all and biology given no place. This however represents only one of the constructions of emotion current at that time, for a biological view of passion also had adherents through the penetration into the wider culture of Galenic humeral theory. Hobbes (1677) translated the same passage:

> "This swelled Achilles choler to the hight
> And made him study what to do were best
> To draw sword and Agememnon kill,
> Or take some time his anger to digest."

Here the model of passion is based in the physiology of the humours, although reason also plays a part in studying "what to do were best". Note the resolution of the anger appeals to a physical process of digesting the excess of anger. For Chapman reason is paramount, but for Hobbes it is secondary to the rise and flow of the humours.

Jealousy is, for Shakespeare both in *Othello* (1604) and *The Winter's Tale* (1610), a consuming passion driven onward by a sense of affronted honour, but in both instances based on error. By the simple expedient of making the jealousy unjustified, Shakespeare becomes subversive of the social and ethical imperatives associated with jealousy. He shifts the passion from its social role into the product of an individual's error which flourishes on the basis of personal vulnerabilities. There is little of Aristotle's educated rationality in the jealousy of Leontes or the Moor. Camillo likens the jealousy of Leontes to a sickness (I, ii, 380) and it certainly has a sudden onset based on a flash of false insight heralded by palpitations (I, ii, 110). Once in motion, these jealousies of Shakespeare are characterised by their imperviousness to reason, at least until after they reach their fatal conclusion. In the Sonnet (number 147) which deals with love and jealousy, Shakespeare also uses the image of emotion as infection which reason like a physician tries to treat, but without success. Shakespeare's jealousy does have something of Homer's infection diverting the sufferer from the path of destiny and duty, but it is a jealousy stripped of any morally or socially redeeming features. This can be contrasted with jealousy as portrayed in the work of Shakespeare's great Spanish contemporary Calderon (1630–81), where the passion is both justified and rational, being as morally admirable as it is murderous.

In Alexander Pope's 18th-century translation of Homer, a view of passion is articulated in which there are two entirely separate realms, that of passion and that of reason, both contending for attention:

> "Distracting thoughts by turns his bosom rule'd
> Now fired by wrath and now by reason cool'd:
> That prompts his hand to draw the deadly sword,
> Force through the Greeks to pierce their haughty lord;
> This whispers soft his vengeance to control".

Achilles now stands buffeted between the twin discourses of reason and passion. Passion prompts violent action, but reason counsels control. In 17-century and early-18th-century Europe, a common view of passion was of what we might now term a 'motivating force', which aroused by an event, drove the affected individual towards action. Passions could cause acts, but such actions were likely to be uncontrolled and inconsistent outbursts. In contrast, when reason governed the response it was likely to be measured and effective. Reason, for most Christians at this time, partook of the divine and had the advantage over passion of being modifiable by experience and open to the direction of education. Passion and reason occupy different realms of discourse and govern alternative modes of responding which lead to different and potentially opposing actions. This view of passion and reason as alternative and opposing still informs much of the commonsense folk psychology of emotion. Jealousy in this construction is entirely separated from reason.

Passion was, for an educated person in the 17th century, best avoided, and reason cultivated as an independent alternative. The view of passion changed during the 18th century: a change which was both influenced and articulated by European philosophers. Hume offers an example. He clearly stated his view of the relationship of reason to passion in *A Treatise on Human Nature* (1740): "Reason is, and ought only to be the slave of the passions and can never pretend to any other office than to serve and obey them . . . tis only in two senses that any [passion] can be called unreasonable . . . where it is founded on false suppositions or chooses means insufficient for the end". Hume's concept of the passions did not, like the previous emotionology, place reason into a separate discourse from passion. In terms of what we would call motivation he ceded primacy to passion, but reason was inserted into the chain connecting passions both to their objects and to their consequent actions. Passions were not mere reactions, but had their origin in pre-existing dispositions and arose in relationship to an object. To use the jargon of our age, Hume's passions were intentional. Reason could in this model influence the choice of object, one could reason about the suitability of someone as a love object or whether that was an event which really justified the emerging jealousy. Further, reason was inserted into the process connecting the passion once formed to any course of action. For Hume reason served the passion by deciding on how best to facilitate its expression.

Passion as understood by Hume does not translate directly into the modern term 'emotion'. It was more closely allied to desire and to the concept of a sentiment. It could influence actions and take part in reactions, but was not the elaboration of biologically determined conditioned or unconditioned reflexes. Hume's views of passion appear somewhat more complex when he articulates his model through specific examples. Love, for example, he views as compounded of three elements: the aesthetic appreciation of beauty, sexual appetite and benevolence. The mixture of these elements may vary, but without all three the passion is not for Hume one of love. The notion of passion as sentiment is illustrated by the 18th-century novelist Fielding in *Tom Jones* (1749) when he wrote: "but it is with jealousy as with the gout, when such distempers are in the blood there is never any security against their breaking out and that often on the slightest occasions". This supposes a passion to be a persisting potentiality, in the very blood of the person, a concept close to the current notion of a trait.

Emotions during the 19th century increasingly acquired the connotations of the transitory and the organic, at least in the literature of science, both scholarly and popular. They shifted from traits to states. They ceased to be compounded of abiding sentiments and desires and became involuntary reactions independent of morality and of those permanent values which characterise a person. Reason's only remaining roles were in helping the individual to avoid situations or attitudes which could trigger the less appetising of these emotional reactions and in mitigating the damaging impulses they engendered. Instinct and biology, reaction and reflex, these became the words appropriate to emotions.

The shift from sentiment to physiological response is only part of the story of how the cultural construction of emotions developed from the 19th century until today. While the scientists, for want of a better word, were exploring ideas of instinct and the biology of emotion, the novelists, quite independently, were redrawing the map of the emotions. Hume's pre-conceptual and pre-linguistic passionate drives were gradually transformed into a complex patterned regularity of dispositional and occurrent feelings, of judgements and actions, such that each element was a necessary part of the whole (MacIntyre, 1988). A recent attempt to deduce a phenomenological description of jealousy employing literary examples derived just such a pattern of dispositions and feelings (Mullen, 1990*b*). The analysis of this material suggested that the elements contributing to the experience of jealousy included judgements, desires, feelings, fantasies and predispositions to behave. The jealousy complex as constructed at the highest cultural level (Tolstoy's

Kreutzer Sonata (1889) and Proust's *Remembrance of Things Past* (1913–22) is far removed from an automatic reaction for it consists of an intentional state of mind in which judgement and fantasy occupy central positions.

Reason re-enters with such models into the very substance of emotions in general and jealousy in particular. Part of the current debate about emotions and the emergence of such trends as the judgementalist and social constructionist views of emotion is about reintroducing, reinjecting this tradition, carried forward until recently largely by novelists, back into the psychological and social sciences.

The evolution of today's jealousy also involved a shift from a passion rooted in socially and morally sanctioned values towards an emotion expressive only of personal desires and preferences. Jealousy in the 'honour' societies was a largely male prerogative connected to public retribution for the damage inflicted on social prestige. In the 18th century jealousy expressed distress at the loss of the person both as a source of gratification and as a possession, but jealousy continued to incorporate a protest against the infringement of ethical and moral values, albeit now more internalised values. The element of loss of property was amply illustrated by the proliferation in 18th-century England of law suits against adulterous wives and their paramours for monetary compensation. Property and marriage had long been intermingled; what was new was the concept of a contract open to renegotiation or a failure to fulfil. The association of jealousy with the treatment of the loved one as a possession has continued as a theme in both popular and scholarly writings. Davis (1936), in his often quoted account of jealousy, claimed "in every case [jealousy] is a fear or rage reaction to a threatened appropriation of one's own, or what is desired as one's own, property".

In Western societies at the end of the 18th century there occurred important changes in the attitude to love and marriage, at least among the more privileged social strata. Love received increasing emphasis as a basis for courtship and marriage. There was nothing new in romantic love; what was novel was viewing marriage as the appropriate and preferred playground for this passion. Love now preceded rather than followed marriage and there was a heightened valuation of heterosexual love and family affection (Gay, 1984, 1986). This is amply illustrated by the family advice manuals which became such a prominent part of middle-class life in the 19th century both in Britain and America (de Gasparin, 1865). In some ways this new emphasis with its idealising of fidelity, particularly female fidelity, would have tended to increase jealousy fears, but more importantly there developed an increasingly hostile attitude to jealousy which was seen as potentially eroding the love relationship and undermining the stability of the family.

Stearns (1989) points out in his history of jealousy in America that the 19th century was riven by conflicting influences on jealousy. On one hand urbanisation broke down the traditional small communities with their mutual enforcement of fidelity by public scrutiny. America gradually abandoned the institutional enforcement of sexual fidelity through its laws against adultery. At the same time the opportunities for romantic and sexual encounters increased and prostitution flourished. Equally, the rise of commercial codes of behaviour made concerns for honour seem anachronistic. Counterbalancing these various forces, which might have tended to heighten jealous anxieties, was the increasing emphasis on the dangers of jealousy. There was an insistence on true love being incompatible with jealousy. The emphasis on female fidelity, coupled with the acceptance of male infidelity, placed the burden for avoiding jealousy squarely on the woman.

Through the 19th century jealousy shifts from being the prerogative of the male to being the problem of the woman. The myth of the 'one great love' central to the 19th-century and early-20th-century emotionology was in practice gender specific. For women it meant what it said, one love, one partner. For men it was interpreted as meaning you, my wife or lover, are the one great love of my life, so all the little transgressions of monogamy are trivial and neither merit nor justify jealousy.

Women were increasingly portrayed as more emotional and less controlled than men and were encouraged to overcome this weakness, particularly to avoid possessiveness and jealousy in the interests of preserving the family. The split between reason and passion reappears embodied in the contrast between the rational male and the emotional female. Jealousy is no longer the expression of offended honour, but of weakness and lack of control stemming from inadequacies of character. Women were increasingly regarded as more prone to emotion, but less prone to carnal desire. Any qualms about double standards with regard to jealousy could be calmed by an appeal to the fortuitous freedom from undue sexual desire which made infidelity for women unnatural and the unfortunate insistence of male urges which made men's indulgence a matter of physical and mental hygiene. The 19th-century view of the bourgeois wife as virtually bereft of sexual desire contrasts with the early-18th-century view of women as more amorous than men and more likely to consume themselves with their passion (Bouce, 1982; Flynn, 1987). Advice manuals, usually written by women for women, in the 19th century regularly praised men who took the trouble to conceal affairs for showing due concern for their wives' feelings. Such manuals tended to urge wives not to make any effort to discover that which knowing could only bring them pain and distress (Stearns, 1989).

Although jealousy was under severe attack in the 19th century both from the forces of the self-declared progressives and the writers of advice manuals, it did not lack champions. The family, at least in theory, remained central. Marriages were about rearing children and infidelity presented a potential threat. A prominent forensic psychiatrist, Charles Mercier (1918), wrote: "the institution of marriage and the instinct of jealousy work for the same end and serve the same purpose. Love selects, jealousy mounts guard to repel third parties from entering the sacred fold". The 20th century saw even this justification for jealousy eroded as the emphasis in emotional and sexual relationships firmly shifted from the family and children to the quality of the couple's relationship. "Does the relationship satisfy my sexual and emotional needs?" became not just an acceptable question, but the central question for many. Jealousy has little place in satisfying anyone's sexual and emotional needs.

Jealousy came under further attack at the beginning of the 20th century from psychologists and psychiatrists who increasingly emphasised that romantic jealousy arose from personal immaturity and reflected a hangover from the sibling rivalries of childhood, with no place in mature adult relationships. Freud and his disciples added to jealousy's burdens with the concept of projection, which emphasises that jealous individuals often had only their own impulses to infidelity to blame which they were projecting onto the innocent partner (Freud, 1955, first published 1922; Jones, 1937).

The picture is further complicated by the version of romantic love promoted by 20th-century popular culture. This love emphasises passionate excitement and enthusiasm which is blind to mundane social constraints. Such love is sustained by novelty. Those in permanent relationships are thrown back into the realm of comparison, which is the realm of jealousy (de Rougemont, 1950), but at the same time, their own opportunities for a further chance at the imagined splendours of new love depends on negating their partner's potential jealousy.

Jealousy approaches the end of the 20th century as an outcast, a problem best avoided, if not avoided then suppressed, and if you fail to suppress it then you become a suitable case for treatment, well if not treatment, at least counselling. A study of 60 counsellors in America (White & Devine, 1991) revealed that their predominant views were that jealousy arose from low self-esteem and excessive dependence on the partner combined with feelings of inadequacy as a lover; in short, a character defect. It leads to excessive demands for attention and sexual exclusivity. Their opinions on the inadequacy of their jealous clients was despite the fact that the couples usually presented in the context of an actual, and acknowledged, rival relationship.

Jealousy has become a pathology of the person suffering it. Gone are its virtues and its justifications. That infidelity conjured it into existence simply allows the therapist, should they be of an old-fashioned bent, to empathise with its emergence before turning to the task of knocking the dependent wimp, who cannot satisfy their partner and is unreasonable enough to demand attention and fidelity, into a shape befitting the late-20th-century person.

What place does the zeal, once central to jealousy, hold for us today? Rawls (1971), a persuasive spokesmen for modern liberalism, wrote "human good is heterogenous because the aims of the self are heterogenous. Although to subordinate all our aims to one end does not strictly speaking violate the principles of rational choice, it still strikes us as irrational or more likely as mad". Rawls is referring in this passage to the subordination of all one's aims to ideological or theological systems, but presumably the same caveat would apply to the overweening enthusiasm of jealousy which from this viewpoint also disfigures the self. Jealousy is nothing if not a protest at a failure to subordinate all of your, and someone else's, aims within a relationship to one end. Zealousness and the pursuit of exclusivity are clearly anachronisms for the liberal individualist. Another philosopher, Heller (1985), expressed this idea about jealousy directly when she wrote "now that freedom has become a universal value idea, hatred felt because of the other's withdrawal of love is irrational indeed".

Current Western society reflects the influence of the market economy, of democratisation, and of the notion of freedom expressed through individual rights. Modernism leaves no place either for jealousy's claims for exclusivity, which offend against individual rights and liberal notions of freedom, or for the jealous person, who is an emotional bankrupt in the market-place of love. Equally, the acceptance of ideas about individual rights as the final arbiter of the good in our society marginalises any claims made on behalf of moral or ethical imperatives which infringe such notions. In the abortion debate, for example, those who oppose claims made on the basis of the rights of the woman to choose, increasingly make their appeal to public opinion in terms of another set of putative rights, those of the unborn child, rather than in terms of moral or divine imperatives. Debates on ethical or social values are replaced by assertion and counterclaim as rights are opposed to rights. Demands for fidelity and exclusivity, central to jealousy, are difficult to sustain on the basis of individual rights, particularly in a liberal society where mutual duties and obligations are dissolved into contracts, actual or implicit. The collective, the social, and even the interpersonal dimensions to which the individual is subject, are lost, to be replaced by the notion of the sovereignty of the individual consumer.

If sexual and emotional relationships are about two individuals entering into an implicit contract to augment their sexual and emotional returns, then jealousy brings with it all the vices and precious few virtues. If we accept the estimates derived from Lawson's (1987) research and review of the literature, up to 50% of women and some 65% of men become involved in extramarital affairs, and a good proportion have multiple affairs. Adultery is now a participation sport indulged in by the masses. Citizens increasingly assume the right to change and vary their erotic attachments. In such a context, and with an ethic in Western society emphasising the rights of fragmented, isolated individuals, how can jealousy be anything but pathology?

There is however a different view of liberal individualism. Hampshire (1989) writes: "A deadening encrustation of conventional classifications of human concerns prevents us looking inwards and from recognising the unnamed exultations and depressions of our inner life for what they are, the revelations of our real nature concealed by our social role". Building on this model of the individual trying to free their rich inner world from the impoverishing influences of tradition and social roles, he offers this construction of love. "Sexual love is associated with a desire to know an individual person with a peculiarly violent curiosity which becomes a desire to enter into another inner world, and to take possession for a time of another person's consciousness, through the body that expresses that consciousness". There could be no more individual and individualistic construction. As the pendulum swings from social and ethical imperatives towards individual freedom so jealousy moves closer to pathology. He is clear that love is no product of reason, "one does not love for a reason any more than one enjoys a joke for a reason, the particularity of the occasion excludes calculation and causal analysis". Does such a construction have a place for jealousy? It leaves plenty of room for envy of those fortunate enough to be the subjects, or objects, of such imaginative curiosity, but it appears to involve no actual claims on the other, to be only "for a time" and to be free of social or traditional encrustations or expectations. This leaves jealousy without a rational basis. Although there is curiosity about the other and their inner world, it is the inquisitiveness of the spectator which regards and explores the other in all their manifestations, physical and psychological. There is no obvious need in this model for reciprocity. It can have Hume's aesthetic and lustful appreciations, but what of benevolence with its desire to promote the happiness of the other? Such love is the love of subject for object, if neither demands nor requires love in return, it desires only "to take possession for a time". The loved one is presumably free to reciprocate the curiosity, or not, for such love would not need to intrude or ask, let alone demand, commitment. Jealousy with such a model would surely be a jarring irrelevance. On the other hand, if love is compounded of curiosity and imaginings its kinship to jealousy would be clear, for jealousy is nothing if not curious and nothing if not driven by a fevered imagination. As Proust (1913–22) wrote: "a little jealousy is not unpleasant . . . for it enables people who are not inquisitive to take an interest in the lives of others, or in one other at any rate".

If we enter sexual relationships not as free and independent contractors, but as members of a society whose values and traditions are not dominated solely by the ethic of the market place; if we enter not as isolated self-sufficient monads, however imaginative, but as dependents seeking some security and reassurance; in short, if we are the human, all too human, members of a tradition which still seeks to realise some of their potential through intimate relationships, then jealousy cannot yet be relegated entirely to a pathology of the passions. But then again perhaps it can and perhaps it should.

This paper could be read as an attempt to rehabilitate jealousy by recalling that it once had both social relevance and interpersonal meaning. Jealousy is about infidelity, and infidelity has a moral dimension. Some commentators claim jealousy is an inescapable part of our nature which can only be controlled by the habit of fidelity (Scruton, 1986). This paper has asserted that fidelity and jealousy are constructed differently at different historical periods and in different cultures, in part because of the changing nature of social and economic realities. The ideology of our age promoted a greater acceptance of polygamous erotic activity and the reputation of jealousy is in eclipse. Moral relativists claim that we can describe the influences of culture on ethical standards, but deny the existence of any transcendent values by which differences could be assessed. Conversely, some would judge this history of jealousy in terms either of ethical perspectives resurrected from the past, or of those dreamed of as future possibilities. The changes in sexual practices in Western culture reflect, in part, the influences of late capitalism's need for mobile atomised labour and the marketing of commodities through the medium of an anonymous eroticism. The deformations imposed on sexuality by the world of profit are often explained not in terms of social forces, but in terms of the victim's own licentious nature. This view sees man's nature as immutable with personal renunciation and strictness offering the only counterbalances to lasciviousness. There may well be biological givens relevant to the world of emotion, but because cultural construction plays a major role, it is change which is characteristic of the history of sexual behaviour and passions rather than the repeated expressions of unvarying nature.

What then of the distinction between normal and pathological jealousy? The problem is the erosion of any area of human experience corresponding to normal jealousy. In our culture jealousy is now regarded not just as problematic or undesirable, but increasingly as unhealthy, as a symptom of immaturity, possessiveness, neurosis or insecurity. To be jealous is to be showing signs of personal, or interpersonal, instability. The symptoms of the psychiatrist are carved out of the totality of human experience by the expedient of attributing them to the causal processes of madness and disorder. This creation of symptoms from phenomena can claim both theoretical and pragmatic justifications, but even the most subtle and sophisticated of clinicians strip much of the cultural and personal meaning from an experience in metamorphosing it into a symptom. What remains of the moral resonance and heroic achievement if the despair of Kierkegaard's (1849) *The Sickness Unto Death* is annexed to a major depression by the criteria of DSM-III-R or is regarded as a symptom of his personal insecurities and relationship problems? The language of symptom claims to understand what really lies behind the other's behaviour but in the process invalidates that behaviour. Our culture makes increasing use of such language to stigmatise the unacceptable. The morally reprehensible, the socially deviant, the personally disruptive, and what remains of old-fashioned evil is likely to be spoken of in the language of our age as a symptom, be it of character defect, social disintegration or developmental disorder. This process is nothing new: one only has to think of the influence of Galen's theory of the humours to realise that biological explanations of social and experiential phenomena are deeply rooted in Western culture. However, between the encroachments of the discourse of psychiatry and that of the wider culture, there now remains little room for jealousy as a valid human activity. With regard to jealousy, whether this is a loss is open to debate. More troubling perhaps, is the progress of a similar process in a range of human experiences such as despair, guilt, fear and nostalgia, whose painful ambiguities make them prime candidates for pathologies, psychiatrically and culturally defined.

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Molecular Biology Symposium

Molecular Genetics of the Major Psychoses: The Role of the Medical Research Council

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Research supported by the Medical Research Council (MRC) is in part initiated in response to proposals from research workers and in part identified by the Council undertaking regular reviews of its portfolio, to identify areas of particular promise, and to ensure that they are adequately supported. One such review, carried out by a group chaired by Professor J. K. Wing, on research in schizophrenia has been published (Schizophrenia and Allied Conditions Committee, 1987), and in the intervening years has been influential in shaping the Council's policy in the field. The report highlighted the molecular genetics of schizophrenia as an example of the ever-increasing number of areas in which an inter-disciplinary approach is essential and in which advances in one field can be exploited in another.

Building on this report and its proposals and reports from adjacent areas in genetics, neurosciences and medical imaging, the Council has identified three major areas of particular scientific promise: the genetic approach to human disease, the neurosciences, and human metabolism. To apply the advances in basic biology to clinical medicine, the Council has also launched the Clinical Research Initiative (CRI). Underpinning all the work on human genetics is the Human Genome Mapping Project (HGMP).

Increasingly, the Council is taking a key role in the development of European strategies in clinical and biomedical research: the Secretary, for example, is currently Chairman of the European Medical Research Councils (EMRC), and the Second Secretary takes the lead in the UK on matters concerning the medical and health research component of the European Community (EC) Framework Programme. The Council's support for the European Science Foundation (ESF) Programme on the Molecular Biology of Mental Illness illustrates their strong commitment to Europe – a commitment which can only increase.

Ways in which the MRC is promoting work on the molecular genetics of the major psychoses

The Council is actively promoting work through the following mechanisms.

The Human Genome Mapping Project

In 1988, the MRC was allocated £11 million over three years as the UK contribution to the international effort on the HGMP. The UK project has now been running for over a year, and a strategy has been developed to complement that of the US programme. While systematic analysis of the total genetic information in man is the long-term goal, the immediate aim of the UK project is to produce worthwhile results in the first five years, and to maximise the return for an annual sum roughly 1/30th of that budgeted for in the US. In contrast to most research which aims to identify specific genes (such as that causing cystic fibrosis), the UK HGMP will adopt a selective rather than a comprehensive approach: genes chosen without reference to disease conditions will be described in sufficient detail to determine whether further investigation is justified. Resources are concentrated on the investigation of the mouse genome which is very similar to that of man, and is easier to work with.

The initiative in the genetic approach to human health

Among the priorities for study in this initiative are the molecular genetics of the major psychoses and of Alzheimer's disease. It has the following general objectives.

(a) *The molecular analysis of disease loci and the characterisation of the mutations which give rise to particular genetic disorders.* The HGMP will lead to the identification of large numbers of candidate disease genes: rapid screening will be developed for the identification and approximate localisation of pathological point mutations before precise definition by sequencing and the development of diagnostic tests. A broad number of approaches will be encouraged.

(b) *The structure and function of the protein products of both normal genes and their mutated counterparts.* Both muscular dystrophy and cystic fibrosis represent good examples of the importance of obtaining information on the structure and function of the protein products of affected genes; for example, the modelling of the structure of the product of the cystic fibrosis gene has recently led to the elucidation of the biochemical deficit in this condition.

(c) *The development of animal models for human diseases.* Transgenic animal models will be further developed as a means of understanding the mechanism of disease formation and possible methods of treatment; a good example – though in a different area of clinical research – is the mouse model for sickle cell disease.

(d) *The clinical application of the genetic approach.* Further research will be undertaken on the safety and accuracy of new methods for antenatal diagnosis; in addition, studies involving the techniques of the social sciences are required to determine the most effective strategies in genetic counselling.

Neurosciences initiative

In parallel with the initiative in the genetic approach to human health, and complementary to it, and to the HGMP and CRI, the Council is developing an initiative in the neurosciences. This has four interlocking themes: the spongiform encephalopathies in man; Alzheimer's disease (including molecular genetics); and the phase II development in the initiative in brain repair at Cambridge and in brain and behaviour at Oxford, for which the Council has already provided the phase I funding and the establishment of an IRC in Brain Repair at Cambridge, for which funding is being sought. The fourth aim of this bid, the molecular genetics of the major psychoses, was prompted by the developments forecast in Professor Wing's report; there are now a number of actual or potentially competitive teams well placed to make a significant contribution to the UK effort. In addition a number of individuals are playing a central role in developing the ESF programme.

The ESF Programme on the Molecular Neurobiology of Mental Illness

This programme, to which the Council as an ESF member organisation is strongly committed, "aims to coordinate the mapping of the human genome for linkage to schizophrenia and affective disorders, in order to identify the genes conferring susceptibility to these syndromes" (unpublished document). The Council has been involved with the development of this programme from an early stage. Last year it contributed £40 million over five years to the core funding, which supports co-ordination, communication, workshops and limited travel for specific purposes. Among the attractions of the programme are the clear co-ordinating structure and the care which has been given in reaching agreement on diagnostic criteria and on the standardisation and exchange of data and material. A further attraction is the development of an initiative from the US National Institutes of Mental Health which will complement that of the ESF.

Research workers wishing to participate in the programme are expected to raise their research funds from other sources, typically their member organisation. The MRC was therefore pleased to provide grant support recently to three UK teams, all of whom will contribute substantially to the programme.

The CRI in clinical neurosciences

Earlier this year, the Council described its plans for the development of the CRI. Its main emphasis forms part of the Council's overall strategy for encouraging major advances in selected areas of basic biology and applying them in clinical medicine. Although the Council's commitment to developing clinical neurosciences as part of the initiative is firm, it is still at an early stage. As part of the development work a committee of the Council's Neurosciences Board (carrying forward and updating some of the work of Professor Wing's report) is at present reviewing the actual and potential research opportunities in biological psychiatry in a national and international context. This review includes consideration of the molecular biological approach to the major psychoses and to Alzheimer's disease; it will also identify locations in which, because of the availability of expertise and facilities, such work is likely to flourish into the next decade.

Ongoing MRC-funded work in its own establishments and in the universities

In recent years, the Council has been supporting work on the molecular genetics of the major psychoses in its own establishments, for example the MRC Human Genetics Unit, the Division of Psychiatry, Clinical Research Centre, and in the universities (University of Edinburgh, University of Wales College of Medicine). While much future work will be co-ordinated within and between the initiatives mentioned above, the Council will continue to consider spontaneous applications which do not fall under any of these headings.

Discussion

The preceding paragraphs, it is hoped, illustrate the Council's increasingly active role in developing research strategies in fields to which it accords a high priority, the ever-increasing interdisciplinary approach to scientific problems, and the interdependence of advances in different fields. A further example is given by the Council's decision to set up a group to examine the present and likely future interfaces between the work of its Neuroscience Board and Cell Board, not least in the field of molecular genetics.

Collaboration

The inevitable corollary of interdisciplinary co-operation and interdependence is collaboration. Specifically in relation to the major psychoses, the relative lack of informative pedigrees worldwide dictates that there must be strict adherence to agreed diagnostic criteria, that cell lines must be shared and, given that the various claims for linkage have not been independently confirmed, that there are routine arrangements for replication. Part of the attraction to the Council of the ESF approach is precisely because it meets these criteria.

Resources

A further corollary is that resource allocation must reflect the most promising and well thought through approaches, irrespective of the field in which they originate. There is a real sense in which advances in the molecular genetics of the major psychoses ride on the back of advances in, for example, cystic fibrosis and muscular dystrophy. At the same time, the molecular genetic approach gives psychiatrists perhaps their most important opportunity ever to enter the 'big science' league. As Lander commented (1988) "psychiatrists have now joined the ranks of experimental geneticists. To be successful in dissecting their particularly complex system, they will need to exploit the full range of tricks of that trade." It is gratifying that the teams supported by the Council are doing just that.

Timescale

The immediate objectives of the ESF programme, provided sufficient families are available for screening, is to describe the extent of genetic heterogeneity and the population frequency of the relevant genes. This could probably be achieved, or significant progress could be achieved, within the five year timescale of the programme. However, the elucidation of the genes conferring susceptibility to schizophrenia and manic–depressive illness, their mode of inheritance, and the nature of the DNA defects, will only provide part of the picture. Other factors, both social and environmental, are known to be important in the aetiology of these conditions; one of the real challenges will be to tease out how they interact. This could take many years.

Another goal concerns the determination of the products of defective gene expression and consequently a scientific basis for the development of rational treatments. This again is likely to be a long-term programme, given that different genetic defects will give rise to different phenotypic expression, and the interaction with other factors.

Counselling strategies for families affected with these conditions should, it is suggested, be approached with caution given the complex interactions mentioned above. The identification of the gene defect in cystic fibrosis has highlighted the difficulty of conveying complex information to the general public sensitively and in a way which allows them to make real choices.

Monitoring

If, as increasingly must be the case, priority areas are promoted as initiatives, it is clearly essential that they are monitored closely to ensure that they are meeting their scientific objectives in the most cost-effective manner, and that these objectives themselves are reviewed to ensure that they remain scientifically valid. The Council has long experience of scientific assessment; it is, however, at present developing new approaches to the monitoring of large-scale activities, such as the CRI and the initiatives in the genetic approach to human diseases and the neurosciences.

Conclusions

The Council is committed to allocating priority to the molecular genetic approach; the major psychoses are an important example. This is reflected by MRC support for the ESF programme and in its new initiatives in neuroscience, and in the genetic approach to human disease: the molecular genetics of the major psychoses are also likely to feature in the clinical neurosciences part of the CRI and are highly relevant to the HGMP.

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Collaborative Strategies in the Molecular Genetics of the Major Psychoses

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Most authorities now agree that a genetic contribution is the best established aetiological factor in manic–depressive illness (McGuffin & Katz, 1989) and schizophrenia (Gottesman & Shields, 1982). In both cases the size of the genetic contribution is substantial, as reflected in estimates of broad heritability (the proportion of total phenotypic variance accounted for by genes) of 60–80%. However, the evidence in favour of a genetic contribution from family, twin and adoption studies tells us that we are dealing with complex conditions which do not have simple Mendelian modes of transmission and in which environmental influences almost certainly play a part. The main debate about mode of transmission has centred upon whether it is entirely polygenic (i.e. dependent upon the action of many different genes, each of small effect) or whether for each of the major psychoses there is a gene of major effect.

Many proponents of the single major effect believe that heterogeneity is probable, so that schizophrenia and manic–depressive illness will each turn out to be a group of conditions, at least some of which show inheritance of the major-effect gene, even if other forms are purely polygenic or even predominantly environmental. The attraction of the hypotheses of a single major effect is that, given the recent advances in recombinant DNA technology, they provide a starting point for a proper understanding of the aetiology of the psychoses. It is now theoretically feasible for any illness which shows inheritance of a major-effect gene but has an otherwise obscure aetiology to detect linked genetic markers, to move from the markers to the gene itself and thence to discover the abnormal (or missing) gene products responsible for the disorder. This 'reverse genetic' approach holds great promise and has already produced strikingly successful results in monogenic conditions such as Duchenne's muscular dystrophy (Hoffmann & Kunkel, 1989) and cystic fibrosis (Riordan *et al*, 1989).

Until fairly recently the search for genes of major effect in complex conditions such as schizophrenia and manic–depressive illness has relied upon studies of the segregation of the disorders in families and the application of statistical methods which compare the theoretical expectations under a variety of models with what is actually observed. The results have largely been disappointing. Complex segregation analysis has provided limited support for inheritance of such a gene in manic–depression (O'Rourke *et al*, 1983; Rice *et al*, 1987) but has provided no clear evidence either for or against this in schizophrenia (Carter & Chung, 1980; Vogler *et al*, 1990). While it seems certain that a 'major' gene on its own cannot explain the transmission of schizophrenia, the possibility of such a gene operating together with polygenic or familial environmental effects cannot be excluded (McGue *et al*, 1985). Thus there is no very convincing evidence in favour of genes of major effect in the inheritance of manic–depression or schizophrenia, but neither is there strong evidence against the existence of such genes.

With this background, and given the very rapid advances which have taken place in mapping the human genome (i.e. in discovering and locating linkage markers throughout the length of the 22 pairs of autosomes and the sex chromosomes), there has been considerable optimism about the potential of genetic linkage studies in complex conditions such as the psychoses. In linkage studies, the usual aim is to study the cosegregation of genetic markers and the disease within families in which multiple members are affected. The tendency for a particular marker allele and the disease to be inherited together within a pedigree can suggest that the disease and the marker locus are close together on the same chromosome. Unfortunately, so far in respect of the psychoses, the results of linkage marker studies have been contradictory and confusing. The promising finding of linkage between manic–depression and markers on chromosome 11 (Egeland *et al*, 1987) was not replicated elsewhere (Detera-Wadleigh *et al*, 1987; Hodgkinson *et al*, 1987; Gill *et al*, 1988) and further studies on the large pedigree in which chromosome-11 linkage was first reported cast doubt on the original findings (Kelsoe *et al*, 1989). There have been similarly conflicting results regarding the claims of X-linked genes for manic–depression (e.g. Mendlewicz *et al*, 1987; Berettini *et al*, 1990). In respect of schizophrenia, the most provocative finding has concerned a report of a linkage marker on chromosome 5 (Sherrington *et al*, 1988). Again, failures of replication followed (Kennedy *et al*, 1988; St Clair *et al*, 1989) and recently reported data, combined with a reanalysis of previously published results, casts serious doubts on the existence of a susceptibility locus for schizophrenia on chromosome 5 (McGuffin *et al*, 1990).

In summary, we have been provided with a potentially powerful new technology for unravelling the aetiology of the major psychoses but are faced with a puzzling set of preliminary results. There is considerable danger that too much energy will be expended in searching a series of temporarily fashionable blind alleys. Against this background, many workers now agree that the way ahead lies in collaborative strategies which provide a more ordered and comprehensive approach. This has resulted in programmes spanning several centres being set up both in Europe and in the US. In this article we mainly focus upon the programme which is being established in Europe under the auspices of the European Science Foundation.

The European Science Foundation programme

Although it is physically microscopic, the human genome in molecular terms is huge. It consists of approximately 3×10^9 base pairs, and two loci which are a million base pairs apart produce roughly a 1% probability of crossing over or recombination in a linkage study. This gives rise to the unit called a centimorgan (cM), by which distance between loci is conventionally measured in linkage studies. Although physical distance and distance in centimorgans is not exactly equivalent, we can roughly say that the human genome is 3000 cM in length. This means that if we were to have regularly spaced markers, about 150 would be needed to detect any disease gene 10 cM or less away from a marker. In practice, markers are not evenly spaced, so that the actual number needed to span the genome effectively is considerably larger (Lange & Boehnke, 1982). It follows that if a systematic search covering the whole genome is to be made for schizophrenia or manic–depression genes of major effect, then the volume of work will be large. Not only will a large sample of informative pedigrees be required, but a large amount of repetitive, time-consuming and costly laboratory work will need to be done. The alternative to undertaking a systematic search is of course to focus on favoured loci where, for example, a hint has arisen as to the existence of a schizophrenia gene because of an observed chromosomal anomaly (Bassett *et al*, 1988) or to concentrate on candidate genes, that is, those genes that encode for a neuroreceptor or other protein which may be involved in neurotransmission. As we have seen, these approaches, together with studies which have attempted to follow up earlier preliminary findings of linkage, have not yielded definitive results. Therefore, the systematic search approach would seem to be essential, but because of its scale, it can only be accomplished through collaborative efforts.

Recognition of this need in 1987 led to the setting up of the Network on the Molecular Neurobiology of Mental Illness by the European Science Foundation (ESF). The aim was to explore the feasibility of a pooling of expertise, clinical material, and technical resources. The enthusiastic participation of researchers from a total of 17 countries suggested that a collaborative venture could be successful and therefore during 1990 a collaborative programme was launched which is destined to last five years and which will co-ordinate the mapping of the entire human genome for linkage to schizophrenia and affective disorder in order to identify genes conferring susceptibility to these illnesses.

The following steps, which will overlap in time, have been defined as tasks of the programme:

(a) to identify a sufficient number of large multiply affected families (about 60 for each illness)
(b) to adopt standardised methods of diagnosis and classification in order to achieve strict diagnostic homogeneity and to establish reliability across centres
(c) to create a databank to store descriptions of pedigrees, clinical information and results of marker typing in order to perform linkage and heterogeneity studies
(d) to establish a code of practice for maintaining confidentiality, assigning right of access to data, and describing ethical issues
(e) to distribute DNA samples of the ascertained pedigrees to collaborative laboratories in order to perform linkage studies with polymorphisms spanned throughout the genome and effect a systematic search.

Given the uncertainties mentioned above about mode of transmission and potential heterogeneity in manic–depression and schizophrenia, the collaborative ESF programme has obvious advantages. To date, some of those positive linkage results that have been difficult to replicate (Egeland *et al*, 1987) have been based on pedigrees which are comparatively isolated genetically and may be atypical. Combining the data from a large number of pedigrees from different geographical areas is of great importance since it will then be possible to decide whether a positive result from one location has any more general applicability. Moreover, from a statistical viewpoint, the advantages of a large sample size are clear.

It seems possible that at least some positive linkage findings in schizophrenia have arisen from the performance of multiple tests using multiple genetic models in the linkage analysis as well as multiple classification criteria (McGuffin *et al*, 1990). The researcher is forced to adopt an exploratory approach regarding both mode of inheritance and the clinical threshold which discriminates between affected and unaffected individuals. Furthermore, a systematic search throughout the genome will inevitably involve hundreds of markers, exacerbating even further the problem of multiple testing. Thus to avoid misinterpretation of positive results, replication becomes vital. This is most easily achieved by having multiple comparable samples which can be analysed both as a large combined dataset and separately as multiple replicates of each other.

Methods

Diagnostic procedures

One of the most important shifts of emphasis in psychiatric research in recent years concerns the methods of establishing precise and reliable diagnostic criteria for the various clinical syndromes. Psychiatric diagnosis is very rarely helped by laboratory or other objective tests and so, in the present state of knowledge, the accurate recording of signs and symptoms provides the only way of making a diagnosis. It is now usual to employ explicit operational criteria for research. These have the distinct advantage of allowing high levels of agreement between clinicians, the essential prerequisite if a study is to be replicated. Unfortunately, several different diagnostic systems are now available which do not always match each other. In the face of such differences it has been decided in the ESF programme to adopt a polydiagnostic approach including DSM-III (American Psychiatric Association, 1980), DSM-III-R (American Psychiatric Association, 1987) and other north American criteria, as well as European systems, and to aim to include the World Health Organization's ICD-10, as soon as it is available.

In order to ensure reliability across centres, the programme will make use of two diagnostic interviews, the Schedule for Affective Disorders, Lifetime Version (SADS-L) (Spitzer *et al*, 1978), and the 10th edition of the Present State Examination (PSE-10) (Wing *et al*, 1990). The decision to adopt two interviews arose because of differences in the stated preferences in researchers taking part in the earlier Network phase of the ESF collaboration. Whereas some workers were already using SADS-L in linkage studies, other centres had expertise in the use of PSE-9 (Wing *et al*, 1974). Consequently, a comparability exercise was carried out as part of the national phase of the programme, and it was shown that the agreement between SADS-L and PSE-10 interviews was highly satisfactory at the level of final diagnostic classification.

It is likely that centres taking part in the ESF programme will use clinician interviewers (either trained psychiatrists or clinical psychologists) rather than lay interviewers and the aim will be to perform personal interviews with all living family members in those pedigrees selected for study. In addition, it is planned to complete an operational criteria (OPCRIT) check-list on all subjects. This provides a way of recording summary clinical data and can be applied where an interview is impossible but where hospital case notes or other written material are available. Having completed the OPCRIT check-list, a computer scoring program generates the classification according to a range of different operational criteria (McGuffin *et al*, 1991). Taken together, the SADS-L or the PSE plus the OPCRIT check-list constitute a common 'minimum dataset' which will be provided by all participating centres in the ESF programme, although it is likely that many centres will wish to add other forms of clinical ratings for their own use.

Ascertainment of pedigrees

As already emphasised, the main thrust will be on studying large pedigrees. Therefore, ascertainment will not be carried out in a strictly systematic way. Consequently, the resulting sample will be of very limited use for segregation analysis or similar statistical studies which attempt to make some general inference about the familial distribution of schizophrenia and manic-depression. However, because the ascertainment will be accomplished blind to the marker genotypes of affected individuals, no biases should be introduced from the point of view of linkage analysis. Already, during the Network phase of the ESF collaboration well over 100 suitable pedigrees have been identified in Europe. However, these are at various stages of completion in the different centres. Thus, in some centres, tracing and interviewing family members has already begun (e.g. in Belgium, France, Germany and Sweden, as well as the UK) and some preliminary results have even been published, whereas elsewhere work remains at the planning stage. However, in nearly all centres, more potentially informative pedigrees have been identified so that the goal of acquiring an adequate sample size is almost certain to be achieved.

The collection of blood, cell, and DNA samples

To ensure permanent access to the DNA from reference pedigrees, lymphocytes will be immortalised and maintained. Thus, after having obtained informed consent, 20 ml of venous blood will be taken from every participating subject. After separation, B-lymphocytes will be transformed by the Epstein–Barr virus to produce permanent B-cell activity. The storage of immortalised cell lines will allow distribution of DNA samples from the whole sample of pedigrees ascertained to collaborative laboratories and will preclude the necessity of returning to families for further blood sampling. In each participating country there is at least one laboratory able to culture cells and to ship lymphoblastoid lines (or DNA extracted from these lines). In some countries, such as the UK, most participating centres are likely to make use of a central repository such as the Public Health Laboratory Service at Porton Down in Wiltshire. Participating laboratories which carry out the molecular genetic studies will receive information about the structure of pedigrees from which the samples are obtained but the laboratory staff will be kept blind as to whether the subject is affected or unaffected by mental illness.

DNA will be submitted to Southern blot analysis (Southern, 1975) in order to perform linkage analysis with the genetic markers spanned throughout the genome. It is likely that most laboratories will want to focus on markers of interest such as candidate genes or markers which have already been implicated in previous linkage studies but, in addition, each laboratory will undertake a systematic search through a specified length of genome using random markers located at approximately 10 cM intervals. Co-ordination of this systematic search will be overseen by the programme's steering committee, with the aim of arriving at a systematic screening of the entire human genome. Currently, there are over 2000 cloned and localised DNA sequences available, of which 200 are multi-allelic and informative in any population. Recent developments, including the use of a variable number tandem repeat (VNTR) markers and repeat adenosine-cytosine (AC) sequences amplified by polymerase chain reaction (PCR), promise to increase the effectiveness and informativeness of linkage marker strategies in coming months (Davies & Read, 1988).

Databank management and linkage strategies

A prerequisite for the smooth running of a collaborative programme is that the data are collected, recorded, and stored in a standard fashion, allowing comparability between centres. A computer program to accomplish this has been developed at the INSERM Genetic Epidemiology Laboratory in Paris. This ensures that clinical data and marker typing are entered correctly and allows the merging of data from multiple centres. The program has a facility of writing out to other programs, such as those used in linkage analysis, and hence reduces the tedium of recoding as well as reducing the risks of coding errors.

In general, likelihood methods of linkage analysis will be employed where the distance between marker and diseased loci is estimated by the lod score method (Morton, 1955). The lod score method, which is based on a sequential strategy, is particularly applicable to the sort of data which will be collected in the programme and facilitates the combining of samples. The computer program LINKAGE will be used to calculate lod scores and where appropriate multipoint analysis will be applied using the program LINKMAP (Lathrop *et al*, 1985). One problem is that mis-specification of genetic parameters (penetrances and gene frequencies) at the disease locus may bias the estimate of genetic distance. Fortunately, such mis-specification does not falsely simulate linkage (Clerget-Darpoux *et al*, 1986). The implication is that for psychiatric diseases where the mode of transmission is unknown, available tests enable linkage to be *detected* but precise *estimates* of the genetic distances between markers and disease are more difficult to arrive at. As a further check against the problems of incorrect specification of mode of inheritance, model-free methods of data analysis such as affected sib-pair tests (Suarez, 1978) will be employed. Finally, in order to test for genetic heterogeneity, the general approach will be to apply admixture tests as implemented in the computer program HOMOG (Ott, 1985).

From locus to gene

As we have implied at the outset, the whole rationale underlying linkage studies is to detect genes of major effect for manic-depression and schizophrenia, to locate such genes precisely, and subsequently to identify the genes themselves and study their gene products. Following on from this, it would then seem feasible (if not necessarily easy) to develop rational therapies. However, we have to temper our optimism regarding 'reverse genetics' with a number of cautions. Firstly, we have already drawn analogy with single-gene disorders where a reverse genetic strategy has provided exciting results, but we need to be aware of the current position in Huntington's disease which provides the best example of a monogenic condition of psychiatric relevance. Here the general location of the gene is known with a high degree of certainty but the precise location is still in doubt seven years after the first report of linkage.

Secondly, we need to remember that linkage methods to estimate distance between loci in cM become very approximate where the mode of transmission of the disease is unknown. Thus, as we have already mentioned, linkage analysis (providing we take into account our other caveats about multiple testing) does not generally result in false positive results because of mis-specification of mode of transmission but can result in inaccurate estimates of the amount of recombination between the marker and the disease locus. Hence discovery of a well replicated linkage marker for schizophrenia or manic–depressive illness might still mean that a comparatively large and ill-defined section of the particular chromosome needs to be studied to define the gene itself.

Thirdly, we need to be aware of the fact that it is just possible, despite the undoubted existence of a genetic contribution to schizophrenia and manic–depression, that only genes of comparatively small effect exist, and that such genes will be undetectable using currently available genetic marker strategies. Although this would be a disappointing outcome, it would not necessarily be a disastrous one. For example, it has recently been argued that most genetically influenced behaviour, including abnormal behaviour, is likely to be polygenic, but even polygenes can probably be detected using association strategies and a search for linkage disequilibrium (Plomin, 1990).

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Molecular Biology Symposium

The Search for the Psychosis Gene

T. J. CROW

The psychoses are mainly genetic in origin

The major psychoses remain an enigma. Affective and schizophrenic psychoses are apparently present (probably at about the same lifetime prevalence of approximately 2%) in all human societies. Yet their aetiology is obscure. While a genetic contribution is acknowledged by most authorities, few accept that genes are a sufficient explanation of causation because: onset is in adult life; psychosis – particularly schizophrenia – is associated with a substantial fertility disadvantage; and most cases lack a family history of illness. But genetic determination has to be considered because onset is determined by chronological age rather than environmental insult (Crow & Done, 1986), adoption away from a family with schizophrenia does not reduce risk of illness, and no plausible environmental precipitant of psychosis has been identified. The fact that psychosis occurs across widely differing climatic, industrial, and social environments without obvious variations in incidence suggests that the disease is relatively independent of the external milieu. The suggestion that birth injury is relevant has been tested in a prospective study (the National Child Development Study) and found wanting (Done *et al*, 1991).

For these reasons, the possibility has to be considered that the aetiology of the psychoses is primarily genetic. Although there have been some advances in our understanding of the nature of the disease process (e.g. the introduction of neuroleptic drugs and the elucidation of their mechanism of action, as well as the discovery of a degree of cerebral ventricular enlargement in schizophrenia), we have no systematic knowledge of the mechanisms of pathogenesis. The conclusion that aetiology is primarily genetic indicates the direction we should take, and suggests that the techniques of molecular biology (including linkage strategies) are the appropriate approach to the problem.

Recent progress in understanding the transmissible dementias

The power of such approaches is illustrated by recent progress in understanding the human spongiform encephalopathies. These diseases can occur in familial forms, but when they do so, they are – as in sporadic cases – transmissible to animals by tissue (Baker *et al*, 1985). They are therefore both genetic and transmissible. The possible nature of the agent has been greatly clarified by the identification by Prusiner and colleagues of the prion gene – the gene that codes for the protein that accumulates in the brains of mice infected with scrapie (for review see Prusiner, 1989). Recently, mutations have been described in the human prion gene in some families with hereditary spongiform encephalopathy (particularly the Gerstmann–Sträussler syndrome), including a base-pair substitution at codon 102 (Hsiao *et al*, 1989) and a 144-base-pair insertion in a conserved repeat sequence in the N-terminal region of the gene (Owen *et al*, 1990). It seems probable that these mutations are instrumental in converting the normal prion protein into a form that is responsible for the onset of this dementing illness in adult life. They provide a clue to the elusive nature of the transmissible agent.

If we conclude that the psychoses are similarly genetic in origin, no fundamental progress in understanding pathogenesis is likely until a gene has been identified. There are two possible strategies: (a) a search for a genetic linkage in order to locate and identify a gene and then by 'reverse genetics' to uncover its gene product; and (b) to use what knowledge we have about the disease process to identify a 'candidate gene'. There is no reason why these strategies should not proceed in parallel; together they may succeed when either separately might fail.

Research strategies: lod score v. sibling pair

While linkage approaches have succeeded in some diseases with a well defined Mendelian mode of transmission (e.g. cystic fibrosis), the psychoses present a number of serious problems.

(a) The phenotype is difficult to define. The use of operational criteria (RDC, DSM–III, etc.) has increased reliability, but it is firmly established that even with a restrictive definition of illness in the proband there is a penumbra of personality disturbance (e.g. schizotypal, borderline and paranoid personality types) that must be regarded as genetically related. There is also the problem that no genetic demarcation can be drawn between 'typical' schizophrenia (e.g. as defined by the Feighner criteria) and schizoaffective psychoses, or indeed between schizoaffective and purely affective psychoses (e.g. Ødegaard, 1972; Angst *et al*, 1983; Gershon *et al*, 1982, 1988). This has led some recent commentators (e.g. Crow, 1986, 1988; Angst & Scharfetter, 1990) to suggest that we are dealing with a genetically based continuum of psychosis.

(b) The mode of transmission is unknown. Although some recent linkage studies (e.g. Sherrington *et al*, 1988; Kennedy *et al*, 1988) have assumed a dominant mode, recessive transmission is also possible. Segregation analyses do not exclude it (Stewart *et al*, 1980) and in one-third of families with two or more affected siblings there are no affected individuals outside the sibship (Crow *et al*, 1989*a*).

(c) There is the possibility of heterogeneity, that is, that different loci are involved in different cases. The variability of the phenotype makes this difficult to evaluate. It can be argued that the failure to achieve an effective subdivision of schizophrenia (e.g. between paranoid and non-paranoid types, or even between schizophrenia, schizoaffective and affective psychosis) does not favour the existence of genetically different forms of psychosis, but this is not a strong argument.

Of the two methods of linkage analysis – the lod score and sibling pairs strategy – that can be applied, the lod score, making use of information from distantly related individuals, has been more widely used and is apparently more powerful. However, when applied to the psychoses it encounters real difficulties with problems (a) and (b) above – the limits of the phenotype and the mode of transmission. To make use of information from relatives one must take a decision on whether they are affected or unaffected. Given that some personality disorders are genetically related to schizophrenia and that the question with respect to the affective disorders is at least open, it is often difficult to say that a given relative is definitely unaffected. A conservative strategy is to adopt the 'penetrance-free' method – the inclusion of affected members only, other relatives being designated 'unknown'. In this case the information extracted from the lod score approach is reduced and it begins to resemble the sibling pair strategy (see below). Uncertainty concerning the mode of inheritance gives rise to difficulties almost as great. What is often done in lod score studies is to vary the definition of the phenotype and the mode of inheritance and then to examine whether different definitions and modes give rise to larger lod scores. In this way a large number of models is being tested, and this needs to be taken into account in probability calculations.

These considerations may in part account for apparent false-positive findings in relation to both schizophrenia (Sherrington *et al*, 1988) and affective disorder (Egeland *et al*, 1987). Doubt on the findings has been cast by subsequent studies in relation to both schizophrenia (e.g. Kennedy *et al*, 1988; St Clair *et al*, 1989) and affective disorder (Kelsoe *et al*, 1989). Most workers assume that the original findings are simply 'false' positives rather than an indication of heterogeneity. A particularly implausible defence of the original findings of Sherrington *et al* (1988) is that while borderline personality should be included in the phenotype of schizophrenia, affective or schizoaffective disorders should be rigorously excluded (Gurling *et al*, 1989).

The sibling pair approach avoids problems (a) and (b) by including in the sample only sibships in which two or more members are definitely affected according to a given definition of illness. The disease status of the parents and other family members outside the sibship is irrelevant. It is necessary to have DNA from one, and preferably both, of the parents. The question to be asked is whether the siblings share alleles at a given locus at or above chance expectation. Because the siblings have been selected only on the basis that they both suffer from disease, if there is a deviation from chance towards sharing alleles that is statistically significant, this is taken as evidence (at the observed probability) that the locus being tested is close to (i.e. linked to) the disease locus. No assumptions are made about the mode of inheritance.

The sibling pair strategy works best with a highly polymorphic locus at which both parents are heterozygous and no alleles are shared between them, such as is the case with the human lymphocyte antigen gene series. The lack of such loci throughout the genome is a limitation, but it is one which is being reduced by the discovery of new types of polymorphism, for example cytosine-adenosine ('CA repeats' or 'microsatellites').

Although it has not yet been generally considered, it may well be that the sibling pair strategy will be the best or maybe even the only way ahead in the genetics of psychosis. Whether or not it will be able to handle the problem of heterogeneity (if it exists) as well or better than the lod score technique remains to be seen.

Co-ordination of research

The issue of sample size and strategy are obviously relevant to the question of the size of the scientific enterprise and how it should be organised. It is apparent to those in the field that although meaningful negative findings can be obtained with quite small numbers of families, large sample sizes may be necessary (although how large is difficult to estimate on account of the uncertainties already discussed), particularly if a number of loci are involved. For this reason collaboration between centres is desirable and may be necessary.

How such collaboration should take place is a matter for informed debate. One proposal is that research should be centralised, for example under the European Science Foundation, or the National Institute of Mental Health in the US. While there are obvious benefits of co-ordination, if such centralisation implies direction from a single laboratory or committee there are also risks (a–c).

(a) Loss of flexibility of approach. For example, until recently only the lod score approach was under consideration in the co-ordinated projects that have been proposed but, as argued above, there are merits in the sibling pair strategy, and this requires a somewhat different approach to family collection.

(b) Overstandardisation of diagnostic criteria. As there are considerable uncertainties regarding the definition of the psychosis phenotype (e.g. whether it should be confined to a restricted definition of schizophrenia as in the DSM–III or Feighner criteria, or whether it should include schizoaffective and affective disorders) the imposition of a uniform definition, as might well result from the decision of a central committee, would be premature and might impede progress.

(c) Stifling of local initiatives. A number of independent linkage initiatives directed at different hypotheses are now in progress. Any more comprehensive co-ordinating structure should seek to encourage rather than supersede or direct these efforts. A co-ordinating committee (such as has been set up under the European Science Foundation) has a role in facilitating communication, proposing standards of information collection, and directing attention to neglected regions of the genome rather than as a command centre.

At least five groups are already active in this field in the UK, and, partly as a result of an initiative by Schizophrenia, A National Emergency (SANE), there is good collaboration between them. Strategies for collection and analysis differ and a number of hypotheses are under investigation. Samples and information are regularly exchanged between groups, and collaborative studies have been arranged. Thus collaboration can arise from the sequential accretion of individual studies as and when a larger sample size becomes necessary to eliminate a particular hypothesis.

Cytogenetic studies and candidate genes

The search for genetic linkage should not pre-empt other approaches to identifying the psychosis gene, such as a search for cytogenetic anomalies that might be associated with psychotic illness and the attempt to identify a candidate gene. Examples of the former approach are the studies that led to attempts to demonstrate linkage on chromosomes 5 (Sherrington *et al*, 1988) and 11 (St Clair *et al*, 1989). Although many expect a candidate gene to be in the class of neurotransmitter receptor or enzyme genes, few such candidates remain following the probable elimination of the D2 receptor as a pathophysiological correlate (Farde *et al*, 1990) and as a linked marker (Moises *et al*, 1989).

A quite different candidate has emerged from recent morphological studies (Crow *et al*, 1989*b*; Crow, 1990). These suggest rather strongly that the brain changes in schizophrenia are asymmetrical and that this asymmetry is specific to psychosis. This raises the possibility that the abnormality in schizophrenia is an anomaly of the genetic determinants of cerebral asymmetry. In that cerebral asymmetry is a late evolutionary development, that is closely related to the human capacity for speech and communication, a genetic basis in an aberration of this gene is plausible. It is proposed by Annett (1985) that the gene for cerebral dominance (the 'right shift factor') is transmitted in an autosomal dominant manner. On the basis of neuropsychological evidence for reciprocal hemispheric deficits in Turner's (XO) and Klinefelter's (XXY) syndromes, I suggested (Crow, 1989) that the cerebral dominance gene might be located in the pseudo-autosomal region – that small region of the sex chromosomes within which there is exchange of genetic material in male meiosis between X and Y chromosomes and transmission occurs in an autosomal manner. For this reason psychoses associated with sex chromosome aneuploidies or other anomalies of the sex chromosomes acquire particular interest.

Conclusion

If, as seems likely, psychosis is primarily genetic in origin, the search for the psychosis gene (or genes) acquires high priority. In parallel with linkage approaches, further work will continue in identifying and excluding candidate genes and searching for cytogenetic anomalies that may provide clues to the location of the psychosis gene.

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British Journal of Psychiatry (1991), 158, 615–623 **Molecular Biology Symposium**

The Genetics of Schizophrenia is the Genetics of Neurodevelopment

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Why is the genetic research into schizophrenia so brainless?

Genes are now accepted as being important in the aetiology of schizophrenia (Gottesman & Shields, 1982; McGuffin *et al*, 1987), and over the past decade the emphasis in genetic research has shifted away from genetic epidemiology to searching the chromosomal DNA for the genes themselves. Despite this increasing technical sophistication, the application of linkage analysis to families multiply affected by schizophrenia has been accompanied by the familiar controversy over the exact borders of the adult clinical phenotype (Sherrington *et al*, 1988; St Clair *et al*, 1989). Indeed, the preoccupation of researchers with the vagaries of the clinical definition has resulted in repeated attempts to use genetic studies to determine the relative validity of different operational definitions of schizophrenia (McGuffin *et al*, 1984; Farmer *et al*, 1987). To us, such studies beg the question of how precisely genes are involved in the aetiology of schizophrenia; after all, genes code for proteins, not for auditory hallucinations in the third person.

Sadly, much contemporary genetic research into schizophrenia ignores the fact that over the past 15 years there have been remarkable advances in the neuroimaging and neuropathology of the condition. It is now evident that abnormalities exist in the temporal lobes of many schizophrenics, and that these have their origins in the early development of the brain (Murray *et al*, 1985, 1990; Weinberger, 1987). In our view, it is no longer sufficient just to fit genetic models to clinical data. Any adequate model for transmission must be compatible with the literature concerning brain structure in both schizophrenics and normals, and with current knowledge of neurodevelopment.

It seems increasingly likely that unravelling the causes of schizophrenia will depend upon understanding what goes wrong in the genetic and epigenetic specification of brain development. To this end, we briefly review the evidence for structural brain abnormalities in schizophrenia, and their developmental origin. Next, we consider the processes involved in neurodevelopment. Finally, we speculate on what is known of the molecular genetics of neurodevelopment with respect to the production of the aberrant neuronal phenotype which underlies the clinical syndrome of schizophrenia.

Structural brain abnormalities and their developmental origin

Neuroimaging studies

Many schizophrenic patients show enlargement of the cerebral ventricles on computerised tomography (CT), although the exact proportion of cases and the extent of the enlargement is still disputed (Owen *et al*, 1988, 1989). Recently, magnetic resonance imaging (MRI) has been applied to schizophrenic patients, and the finding of increased ventricular size in a proportion of schizophrenics confirmed (DeLisi *et al*, 1990). In addition, MRI studies have shown reduced volume of temporal lobe structures and of the hippocampus in particular (Suddath *et al*, 1989; Bogerts *et al*, 1990*a*). Nasrallah *et al* (1990) reported an inverse relationship between hippocampal size and lateral ventricular volume.

Monozygotic (MZ) twins discordant for schizophrenia have been examined to ascertain the relative importance of genetic and environmental factors in the causation of the structural brain abnormalities. Thus, Reveley *et al* (1982) showed that, on CT, schizophrenic twins have larger ventricles than their non-schizophrenic MZ co-twins. More recently, Suddath *et al* (1990) examined 15 pairs of discordant MZ twins and confirmed with MRI that the illness is associated with enlarged lateral and third ventricles, reduced volume of the left temporal lobe, and smaller hippocampi.

A developmental lesion

Twin studies show that neither schizophrenia nor the associated neuroradiological abnormalities can be explained by genes alone; environmental agents must be involved. Obstetric complications (OCs) are more common in schizophrenics than in other psychiatric patients or normal controls (McNeil & Kaij, 1978; Lewis & Murray, 1987; Eagles *et al*, 1990), and a number of studies suggest that OCs are associated with ventricular enlargement in adult schizophrenics (Cannon *et al*, 1989; Lewis *et al*, 1989). OCs late in pregnancy or at delivery are the most likely to be detected, but they may merely be markers of some covert event earlier in development (McNeil, 1987). Whatever the exact timing, the comparative rarity of OCs in the histories of schizophrenics with similarly affected relatives compared with non-familial schizophrenics (Lewis & Murray, 1987; O'Callaghan *et al*, 1990) indicates they are unlikely to be a secondary consequence of a purely genetic defect in neuronal development (Owen *et al*, 1988; Goodman, 1988).

Minor physical abnormalities (MPAs) are trivial abnormalities in ectodermal development (e.g. malformed ears or palate). MPAs occur in excess in patients with developmental disorder (Smith, 1976). Schizophrenic patients also show more MPAs than expected (Gualtieri *et al*, 1982; Guy *et al*, 1983; Green *et al*, 1987). As the central nervous system (CNS) is itself an ectodermal derivative, MPAs may reflect events which also occur in the CNS. Like OCs, MPAs implicate a pathological process operating very early in life. Unlike OCs, they are found more frequently in familial schizophrenics (Waddington *et al*, 1990), and the possibility that MPAs reflect genetically controlled events is discussed below.

Thus, several lines of evidence suggest that pathogenic processes in schizophrenia are active many years before the onset of the florid psychotic illness, during the vulnerable period when the brain is still developing. Therefore, in order to understand how the abnormalities seen in the brains of some schizophrenics may have arisen, it is necessary to understand the processes which determine brain development.

Brain development and the neuropathology of schizophrenia

The development of the human brain from a group of cells to the adult organ is a staggering undertaking. In the human cerebral cortex alone there are around 10^{10} neurones and perhaps 10 times as many glial cells (Blinkov & Glezer, 1968). The neurones, with over 10 000 connections per cell (Kuffler *et al*, 1984), constitute the computational networks of the brain; glial cells have a variety of supportive functions in the adult CNS and play a primary role in neurodevelopment (Kuffler *et al*, 1984). Despite its complexity, neurodevelopment can be considered in terms of the basic principles of developmental biology: cells proliferate, migrate, differentiate into mature forms, and, lastly, a proportion die before the adult pattern is established. The process of selective cell death is particularly important, and Kolb (1989) has compared neurodevelopment with the creation of a sculpture, either by chiselling away unwanted parts of a large block, or by starting with granules of sand and glueing them together to form the desired shape. The brain is formed using both strategies: firstly, building up a prototype with excess cells and connections, and then honing it down to the desired construction. In the human embryo, at around 14 days, chemical signals cause ectodermal cells to divide and form a sheet known as the neural plate. This invaginates along the length of the embryo, folding it on itself to form a hollow tube which is the precursor of the entire CNS. Elongation and circumferential growth create the subdivisions of the adult CNS. Proliferation, migration and differentiation occur in the radial plane, the thickness of the tube, and give rise to the laminated cell structures characteristic of the regions known to be abnormal in schizophrenia.

Cell proliferation

Both neurones and glia are generated in proliferative zones which appear adjacent to the inner wall of the neural tube. Mitosis and cell division always occur away from the ventricular surface of this zone, and newborn cells accumulate outside the ventricular zone, in a centrifugal fashion. The basic structure of the spinal cord (Nornes & Das, 1974) and the CA1, CA2 and CA3 regions of the hippocampus (Nowakowski & Rakic, 1981) develop in this manner, with the original young neurones being displaced away from the ventricular surface as more are produced by the ventricular zone.

Thus, neurones and glia are produced as clones from a small number of autonomous progenital cells (Wetts & Herrup, 1982; Temple & Raff, 1986).

We noted earlier that MRI studies have shown decreased volume of the temporal lobes and hippocampi of schizophrenics. Neuropathological studies confirm this (Bogerts *et al*, 1985, 1990*b*; Falkai & Bogerts, 1986; Jeste & Lohr, 1989). The question as to whether the decreased volume is due to developmental or degenerative processes is partly resolved by looking at glial cells. Gliosis is the usual glial-cell reaction to neuronal damage, except in the foetus; its absence in most, but not all, schizophrenics (Falkai & Bogerts, 1986; Bruton *et al*, 1990) raises the possibility of a defect in cell proliferation in the developing brain, particularly affecting the hippocampal formation. This is a phylogenetically ancient structure which develops exclusively from the ventricular zone (Nowakowski & Rakic, 1981). The decreased cell numbers found in the hippocampi of schizophrenics (Falkai & Bogerts, 1986; Jeste & Lohr, 1989) may be a consequence of abnormal control of proliferation in the ventricular zone, either generally or affecting cells destined for a specific site.

Cell migration

Young cortical neurones migrate across an intermediate zone to produce the cortical plate from which the mature cerebral cortex develops. The cells forming the cortical plate are arranged in such a way that the first to be generated remain nearest to the proliferative zone and subsequent generations are to be found progressively further away. This 'inside out' pattern of neurogenesis is characteristic of the development of laminated structures (Hickey & Hitchcock, 1984), and clearly derives from a more complex migratory process than the passive displacement of cells destined for the spinal cord. How is this migration controlled?

Neurones en route to the cortex and cerebellum are intimately associated with elongated glial cells throughout migration (Rakic, 1971). These cells are known as radial glia because of the way in which their processes stretch from the ventricular to the pial surfaces like the spokes of a wheel. Radial glia act as guides for migrating neurones, providing both support and directional information (Eckenhoff & Rakic, 1984). Their interaction with neurones involves several stages. Initially, the young neurone becomes opposed to the glial fibre. Then it migrates along the glial fibre, always away from the proliferative zone, through the intermediate zone to the cortical plate. Finally, contact between the two cells is severed at the correct time and, therefore, position. Once this has occurred, another young neurone from the proliferative zone becomes attached to the fibre and remains so until it has passed the position of its predecessor, thus establishing the columnar architecture of the cortex.

If neuronal migration is disrupted, an abnormality in cell position results. Kovelman & Scheibel (1984) claimed to find such positional disarray of the normally regimented ranks of pyramidal neurones in the CA1/CA2 regions of the hippocampus in schizophrenics. Two subsequent studies failed to find a statistical difference in neuronal disorganisation between schizophrenics and controls, although one of these did report greater disarray among those schizophrenics with a more severe psychosis (Altschuler *et al*, 1987; Christison *et al*, 1989). More definitely, Jakob & Beckman (1986) noted, and Falkai *et al* (1988) confirmed, that pre-alpha neurones normally located in the superficial layers of the entorhinal cortex are displaced deep to their expected position in the brains of some adult schizophrenics. This was particularly true of those cases which present before age 25 years.

A defect in control of embryonic neuronal migration is an appealing explanation, particularly since a variety of rare disorders of cell migration have been associated with schizophrenia (Reveley & Reveley, 1983; Lewis & Mezey, 1985; Lewis, 1987; Blackshaw & Bowen, 1987). Since it is the interaction between neurones and glia that determines migration (Hatten, 1990) it is possible that a defect may lie at their interface. It has been suggested that this cell–cell interaction may be affected in schizophrenia (Conrad & Scheibel, 1987; Nowakowski, 1987) and that the mechanism may involve cell surface glycoproteins called cell adhesion molecules (CAMs); these are discussed later.

Differentiation and connectivity

Differentiation of cells in the nervous system is extraordinarily complex, and includes the generation of many cell types and formation of precise connections. Abnormal cell types have not consistently been described in schizophrenia, but abnormal connections have been considered a possible cause (Randall, 1983; Goodman, 1989). Connections are formed by growing axons which have specialised structures at their tips known as 'growth cones'. These are highly dynamic (Raper *et al*, 1988) and axonal growth is dependent upon the stabilisation of structural microtubules within them, a process itself dependent upon regulatory proteins (Matus, 1988). The factors which guide the growth cone towards the correct target include mechanical constraints, growth over pre-formed glial structures, electromechanical forces, and attraction towards sources of specific chemicals, probably CAMs (Thanos *et al*, 1984; Trisler & Collins, 1987). The growing axons seem to feel or 'sniff' their way to their targets (Raper *et al*, 1988; Stirling & Summerbell, 1988). Once a pioneer reaches its target, changes in CAM expression on its surface attract other axons to follow.

Patterns of connections are further honed after birth by the function of the network itself. For example, in the visual system, the detailed connections of axon terminals in the lateral geniculate nuclei and visual cortex depend upon the quality of visual experience during a critical neonatal period (Hubel & Wiesel, 1970; Greenough *et al*, 1987).

Myelination of axons, a function of mature oligodentroglia, continues well into adolescence (Yakovlev & Lecours, 1967). The ongoing process of myelination provides one way of explaining the late behavioural consequences of an early brain lesion in schizophrenia (Randall, 1983; Weinberger, 1987). For example, Benes (1989) has shown the appearance of strikingly increased myelination of the subicular and pre-subicular regions during late adolescence. These structures have a strategic location within the corticolimbic circuitry of the brain; the subiculum receives its principal input from the CA1 sector of the hippocampus, a sector which we noted earlier may contain abnormally positioned cells in schizophrenia. Many authorities believe that a dysfunction of the septo-hippocampal system is crucial to the genesis of schizophrenic symptoms. Thus, myelination of parts of this circuitry may in some way permit a pre-existing but latent defect in the hippocampus to become manifest clinically.

Cell death

It was formerly thought that the factors discussed above combined with great economy to produce the desired connections between cells. This no longer appears to be the case. Developing axons form many transient connections during development. These exuberant connections are eliminated by several types of regressive processes and between 30% and 40% of all cells generated in the nervous system die by the time it is mature (Cowan *et al*, 1984). This process is dependent upon trophic factors such as nerve growth factor (NGF) produced by target cells as well as by the formation of functioning connections (Oppenheim, 1981; Henderson *et al*, 1986). Thus, like birds competing for food in the winter, those neurones that lose out in the race to target cells die. Similarly, some axons' collaterals are pruned (O'Leary & Stanfield, 1985) and terminal arborisations of axons or dentritic trees shrink (Wiesel, 1982), with consequent decreases in synaptic densities (Oppenheim, 1981; Rakic *et al*, 1986).

Benes *et al* (1986) found neuronal density to be lower in schizophrenics in layer IV of the pre-frontal cortex, layer V of the cingulate gyrus, and layer III of the motor cortex. They suggest that these abnormalities could have arisen from "an accelerated process of neuronal drop out early in life, perhaps related to a perinatal insult". Benes & Bird (1987) then reported increased numbers of vertical axons in the cingulate cortex of schizophrenics, a finding compatible, as a compensatory phenomenon, with decreased death of primitive neurones. Similarly, Deakin *et al* (1989) attribute the abnormally dense glutamatergic innervation which they postulate in the frontal cortex of schizophrenics to "an arrest or failure of the process by which transient callosal projections normally are eliminated during development". When extra targets for growing axons are provided experimentally, neurones normally destined to die then survive; such a process could provide another explanation of persistence of the heterotopic pre-alpha cells in schizophrenia, discussed above.

Genetic controls in neurodevelopment

At least 30% of human genes are expressed exclusively in the brain (Sutcliffe *et al*, 1984). However, there are far more cells in the CNS than there are genes, and even this massive commitment is not enough for the nervous system to be organised in a point to point fashion under direct genetic control. Instead, brain development involves a cascade of genetic and epigenetic controls, with genes regulating each others' expression, and interacting with local environmental factors to produce an array of regulatory proteins.

We are beginning to learn about the control of the early stages in the process whereby cells of the ectoderm become committed to forming the human CNS. Work on Drosophila has identified several genes whose inactivation leads to a striking hyperplasia of the CNS (Ghysen & Dambly-Chaudiere, 1989).

It appears that 'neurogenic' genes allow a subset of ventral ectodermal cells to become neuroblasts, and then, through lateral inhibition, impose a different fate on the neighbours of the committed cells by preventing them from also becoming neuroblasts. Such genes are highly conserved through phylogeny and it seems quite possible that similar mechanisms of cell specification operate in the human embryo.

'Homebox' (Hox) genes comprise a multigene family whose members play an important role in many animal phyla, specifying patterns in development and particularly the formation of segments. Segmentation acts like a simple ground plan of development; once segments have formed, each one then goes on to develop specific structures, again dependent on gene expression. The original pattern may be obscured as development increases in complexity. Parts of the CNS develop from a simple segmented pattern, so it might be expected that Hox or related genes will modulate particular patterns of gene expression and regional differentiation (Schugart *et al*, 1989). For example, in the mouse, expression of four Hox-2 genes in the developing hind brain shows a segmented pattern, with the limits of expression of these genes being coincident with structural segment boundaries (Wilkinson *et al*, 1989*a*). Thus, these genes appear to be specifying segment phenotype in the hind brain.

Interestingly, the sequence of these Hox-2 genes on the chromosome is the same as their sequence of expression in the tissue. This arrangement, found for all Hox genes, probably occurs as the genes are activated in temporal sequence during development. Rakic (1988) suggests that in primates at least two sets of such regulatory genes control the formation of the basic cytoarchitectonic structure of the cortex. One set parcels proliferative units within the ventricular zone into a protomap of basic cytoarchitectonic areas in the cortex and controls the number of young neurones generated. A radial glial scaffolding simply translates this map from the ventricular zone to the expanding cortical plate. After the number of proliferative units is established, other homeotic selector genes regulate the individual cellular phenotypes within that unit.

A family of Hox-like genes, the POU-domain genes, has been described (He *et al*, 1989). These exhibit distinct temporal and spatial patterns of expression during brain development in the rat. Certain of these genes (Brn-2 and Tst-1) are widely expressed in the proliferative zone and early cortical plate. Later their expression is restricted to different layers that reflect the mature laminar patterns. Thus, these genes appear to be involved in the generation of neurones in the proliferative zone and in their subsequent migration to the cortex. Both these processes may go awry in schizophrenia (Jeste & Lohr, 1989; Falkai *et al*, 1988) and one can see how a mutation in such a gene could underlie the neuronal phenotype found in the condition.

Other types of genes are implicated in mammalian embryonic development; these include zinc-finger genes and oncogenes. Zinc-finger genes, such as Krox-20 in the mouse, encode a type of protein found in several transcription factors and so it is likely that the protein encoded by Krox-20 regulates the expression of other genes (Chavrier *et al*, 1988). In the mouse hind brain, expression of Krox-20 parallels but precedes the segmented structure seen during development (Wilkinson *et al*, 1989*b*), consistent with the gene having such a regulatory role. Most oncogenes are involved in self-proliferation, some in cell differentiation. Greenberg *et al* (1990) have identified a T-cell oncogene on chromosome 11p which is expressed segmentally in the mouse hind brain early in embryonic development and subsequently in other tissues, including certain cell layers of the hippocampus. Genes such as this that are expressed in the hippocampal formation are particularly interesting in view of the post-mortem studies of schizophrenia mentioned above which implicate a developmental abnormality in this structure (Jakob & Beckman, 1986; Falkai *et al*, 1988).

We have some knowledge of the control of hippocampal and cerebellar development in mice because these structures are predictably affected by well characterised single gene defects causing abnormal cellular migration and heterotopic cells (Caviness & Rakic, 1978; Nowakowski, 1987). In NZB/BINJ mice, young neurones migrate too far, while in the Hld, dreher and reeler mice, the abnormally positioned cells have not migrated far enough. This is reminiscent of the cytoarchitectonic findings in schizophrenia, and several authors (Nowakowski, 1987; Conrad & Scheibel, 1987) have commented on the possibility that these mutations may serve as models for some process which occurs in the disorder.

Cell adhesion molecules

As mentioned previously, migration of young neurones depends upon their interaction with radial glia. This interaction is mediated by CAMs, which are expressed on cell surfaces and which bind to each other, thus linking cells together (Edelman, 1986). CAMs are a large family of glycoproteins whose functions are crucial to the migration of cells; in the adult, CAMs maintain the mature form (Crossin, 1989). The study of CAMs and morphology (Edelman, 1988) is beginning to explain the paradox by which a one-dimensional genome can control the formation of three-dimensional structures. Over 30 different CAMs have been described, comprising these main families. Some have a variety of forms (Murray *et al*, 1986), resulting from changes in messenger RNA originating from a single gene (an epigenetic mechanism), and changes in the amounts of sialic acid associated with the protein core (a post-translational modification).

The role of CAMs in cell migration may be of relevance to schizophrenia. In normal development, cerebellar granule cells assume a complex, regular configuration by translocating along specialised radial glial cells (Rakic, 1971). In the weaver mouse mutant, this process fails to occur and young granule cells do not migrate. At least four separate CAM adhesion/recognition systems are involved in granule cell migration (Lindner *et al*, 1983; Hatten *et al*, 1984, 1986; Hoffman *et al*, 1986; Edmondson & Hatten, 1987) with both these neurones, and the glial cells, expressing adhesion molecules. One of these, termed 'astrotactin', is expressed by granule cells and is necessary for migration (Edmondson *et al*, 1988). Weaver-mice granule cells express less than 5% of the normal granule level of astrotactin and, when examined in microculture systems, weaver granule cells fail to migrate along wide-type astrocytes. However, a combination of weaver glia and wild-type granule cells results in migration as usual. There appears to be a standard mechanism for neuronal migration in different regions of the brain (McConnell, 1988; Hatten, 1990), with the genetic route map being expressed in the neurones. If this holds true in studies of other mutants where migration is abnormal, then this may have implications for schizophrenia.

Cell adhesion molecules are also important in the establishment of connectivity. Laminin, a CAM associated with the extracellular matrix is expressed along the pathway of the embryonic chick optic nerve while axon outgrowth is occurring (Cohen *et al*, 1987), but the expression ceases once the nerve has developed. Interestingly, in species such as goldfish where nerve regeneration in adults occurs, laminin continues to be expressed throughout life (Liesi, 1985). Development of precise connections may also depend upon the presence of CAMs. By keeping axons tightly bundled while they grow, the task of reaching the correct targets is simplified, just as it is easier to thread a needle with a fresh thread rather than a frayed one. Finally, in the genetic mutant mouse 'staggerer', where cerebellar connectivity is abnormal, Edelman & Chuong (1982) demonstrated a specific abnormality in the major neuronal adhesion molecule, N-CAM. N-CAM is associated with a large amount of polysialic acid in the normal embryo and this proportion decreases markedly as development proceeds, rendering N-CAM in the adult more adhesive. In the homozygote staggerer cerebellum, this embryonal to adult conversion did not occur by 21 days after birth, and as a result the neuronal circuitry was abnormal.

In such processes we now know the gene products involved, CAMs, where and when these products are expressed, the effects of perturbations of that expression and, for N-CAM at least, we know the locus of the gene on human chromosome 11 (McConville *et al*, 1990). It is hardly surprising that researchers have already looked at CAMs in schizophrenia. Lyons *et al* (1988) measured N-CAM in the serum and cerebrospinal fluid (CSF) of patients with schizophrenia and found increases in a serum fragment of N-CAM compared with controls. Adult CSF is, however, a long way from the micro-environment of hippocampal development, and caution must be used in interpreting the significance of such CAM changes.

Cell adhesion molecules may have a more prosaic use to psychiatric geneticists. It is quite possible that some of the minor physical abnormalities (MPAs) common in schizophrenics are due to processes involving abnormal ectodermal expression of CAMs. If this is so, then they may have some genetic aetiology in common with the perturbed neurodevelopmental processes we believe to be fundamental to schizophrenia; that MPAs are more common in familial than non-familial schizophrenia (Waddington *et al*, 1990) lends some support to this notion.

As more genes for CAMs become localised, they join other genes important in neurodevelopment as attractive candidates for linkage analysis and association studies. Kennedy *et al* (personal communication) have already excluded linkage to schizophrenia of the Hox-2 gene cluster on chromosome 17. From the neuropathological findings in schizophrenia we would predict that genes expressed later in development may be more likely candidates. With regard to CAM genes, we have noted that considerable alterations occur in both the messenger RNA and the nascent CAM protein, so the area is complex.

A necessary caveat in explaining the neurobiological findings in schizophrenia only in terms of molecular biology and genetics, is that we know that environmental factors are involved in the disease and in some of the models discussed. Herndon *et al* (1971) and Nowakowski (1987) have shown that identical neuronal phenotypes to those which result in the mutant mice can be produced by environmental hazards such as ionising radiation, excessive alcohol, or maternal viral infection, provided these factors operate at the critical period of brain development. Mednick *et al* (1990) have reported that Helsinki residents who were in their second trimester of foetal development during the 1957 influenza-A epidemic had a significantly increased risk of later schizophrenia. Conrad & Scheibel (1987) suggest that neuraminidase-bearing viruses such as influenza could interfere with the sialation of CAMs in a way analogous to the disrupted embryonal–adult conversion of N-CAM seen in staggerer mice. Finally, hippocampal pyramidal cells are very vulnerable to mild anoxia/ischaemia (Brown & Brierley, 1973; Jorgensen & Diemer, 1982) and such damage could permanently alter hippocampal structure.

Conclusion: putting the brain back into genetic research

It is evident that in seeking to understand the genetics of schizophrenia we should not expect to find a gene that codes directly for first-rank or negative symptoms. Instead we may find a defect in the control of neurodevelopment whose end result is a set of structural changes which predispose to later schizophrenia. The complexity of brain development might permit a variety of genetically determined events to produce a similar morphological and clinical phenotype; environmental interference with the same developmental processes may mimic the pathological and psychopathological picture.

Such a hypothesis implies that schizophrenia is aetiologically heterogeneous (Murray *et al*, 1985); indeed, it is possible that it may occur only when an individual inherits several contributory genes or when an individual with one or more abnormal genotypes also suffers foetal adversity. This view is compatible with recent suggestions that familial data in schizophrenia are best explained by some gene–gene or gene–environment interaction (Risch, 1990).

The practical implication of an aetiological model such as we have outlined is that the clinical syndrome of schizophrenia (or even of the schizophrenia spectrum) may not be the most appropriate phenotype on which to carry out genetic analysis – it may be too remote from gene actions. Certainly, it is now obvious that attempting to use heritability data derived from twin studies to determine the most 'genetically valid' definition of schizophrenia is no more useful than it would be to argue over the nature of the chest pain accompanying myocardial infarction in an attempt to resolve the complex genetics of lipid transport. Furthermore, it may not be sensible to carry out linkage studies which take a behavioural definition such as the DSM–III criteria of schizophrenia (or some wider or narrower equivalent) as the only appropriate phenotype. It makes more sense to incorporate measures of cerebral structure or function into the study, and then also seek linkage with the relevant endophenotype (e.g. abnormal temporal lobe structure).

It remains unclear whether molecular genetic techniques, such as the lod score method in multiply affected families, will ultimately prove as successful in schizophrenia as they have in so many medical disorders. What is no longer in doubt is that psychiatric geneticists need to focus more of their effort on understanding the molecular rules governing neurodevelopment and how these may be transgressed in schizophrenia. The brain needs to be put back into genetic research in schizophrenia!

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Evidence for a Pseudo-autosomal Locus for Schizophrenia Using the Method of Affected Sibling Pairs

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A susceptibility locus for schizophrenia in the 'pseudo-autosomal' region has been proposed on the basis of the reported excess of sex-chromosome aneuploidies (e.g. XXY and XXX) among patients with schizophrenia and the finding that schizophrenic sib-pairs are more often of the same than of the opposite sex. This hypothesis has been tested in 83 sibships with two or more siblings fulfilling Research Diagnostic Criteria for schizophrenia or schizoaffective disorder. Alleles at the pseudo-autosomal telomeric locus DXYS14, which is unlinked with sex, were analysed using the method of affected sib-pairs. Affected sibs shared alleles at DXYS14 more frequently than expected by random Mendelian assortment, supporting genetic linkage between DXYS14 and schizophrenia.

A genetic contribution to the aetiology of schizophrenia is supported by twin and adoption studies (Gottesman & Shields, 1982; Kety, 1983) although the mode of inheritance remains unclear (Kendler, 1988). On the basis of an excess of sex-chromosome aneuploidies (e.g. XXX and XXY) among patients with schizophrenia and reports that schizophrenic siblings are more often of the same than of the opposite sex, a genetic locus for schizophrenia within the pseudo-autosomal region of the sex chromosomes has been proposed (Crow, 1988). The pseudo-autosomal region is that part of the distal ends of the short arms of the X and Y chromosomes that undergoes recombination in male meiosis (Burgoyne, 1982; Simmler *et al*, 1985; Rouyer *et al*, 1986). A disease allele located here will show a tendency to be transmitted from a father to either sons or daughters depending on whether it is on his Y or X chromosome respectively, with the result that affected sibs tend to be of the same sex (see Discussion). As predicted for pseudo-autosomal transmission, concordance by sex in siblings with schizophrenia is present in families with a paternal and not with a maternal history (Crow *et al*, 1989), a finding that is difficult to explain in terms of ascertainment bias, an earlier explanation of same-sex concordance (Sturt & Shur, 1985). The criticism that the finding is dependent upon an excess of males in the series (Curtis & Gurling, 1990) has been addressed and, within the limitations of the sample, discounted (Crow *et al*, 1990).

Here we have tested the pseudo-autosomal hypothesis directly using a highly polymorphic DNA marker at the telomeric end of the pseudo-autosomal region.

Most psychiatric linkage studies to date have utilised the lod-score method in extended pedigrees; sibling-pair methods have been little used. However, the lod-score approach to schizophrenia is complicated by the unknown mode of inheritance, incomplete penetrance, and variable age of onset. Such likelihood methods of linkage analysis were developed, and appropriate significance levels determined, for single-gene disorders showing clear Mendelian inheritance: no such mode of inheritance has been demonstrated in schizophrenia. Moreover, the reduction of risk for the more distant relatives of schizophrenic probands is larger than expected for a Mendelian disorder even if several, non-interacting genes are involved.

Interaction between several loci has been proposed as a more likely model (Risch, 1990), and in this situation methods of analysing affected pairs of relatives may be particularly suitable (Gershon & Goldin, 1987; Ott, 1990). In addition, the problem of classifying individuals with schizophrenia spectrum disorders (Ingraham & Kety, 1988), bipolar and unipolar affective illness and other psychiatric illnesses that are frequently seen in schizophrenic pedigrees presents major difficulties. To allow for these uncertainties, lod scores are maximised over several models of the phenotype but the appropriate level of significance is then difficult to determine.

For these reasons we chose an analysis of affected sib-pairs. Because only clearly affected individuals are included, the problems of disease definition, variable age of onset and incomplete penetrance are circumvented. No assumptions are made concerning the mode of inheritance.

Findings on a group of 40 sibships were presented at the 10th Human Genome Mapping Conference at Yale University in June 1989 (Collinge *et al*, 1989). The present report includes an enlargement of that sample.

Method

Eighty-three sibships each including two or more members with schizophrenia were drawn from three sources of pedigrees: (a) a series collected in the course of routine clinical work (that included a number of research investigations) at a district general hospital (Northwick Park) in Harrow and by contacts with other clinicians, and the National Schizophrenia Fellowship (21 families); (b) a series collected from January 1985 to the present, across the USA by recruitment of families with more than one schizophrenic member (46 families) (Delisi *et al*, 1987; Crow *et al*, 1989); (c) sibships collected in Dublin (AL and CL) (5 families), Edinburgh (with the help of Drs D. H. R. Blackwood, D. M. St Clair and colleagues, 6 families), Cardiff (Dr M. Sargeant and Professor P. McGuffin, 2 families) and the Institute of Psychiatry (Professor R. M. Murray and Dr V. Nimgaonkar, 2 families) and at the Middlesex Hospital (Drs H. D. Gurling and T. Read, 1 family).

Psychiatric interviewing and diagnosis was performed using the Schedule for Affective Disorders and Schizophrenia, Lifetime version (SADS-L; Endicott & Spitzer, 1978) for the US and Dublin samples and the SADS-L supplemented by the Present State Examination (PSE; Wing *et al*, 1974) for the Northwick Park sample, and by review of available case notes, blind to results of the laboratory work. Criteria for inclusion were (a) that there were at least two siblings within each family who had suffered from a psychiatric illness of sufficient severity to require hospital admission, and (b) that the illness met the Research Diagnostic Criteria (RDC; Spitzer *et al*, 1978) for a diagnosis of schizophrenia or schizoaffective disorder. All sibling pairs had at least one parent available for sampling. Well siblings were also interviewed and sampled when available.

Table 1
Sex composition and IBD scores of affected sibships

	No. of sibships	Sex composition	IBD scores possible	No. of times each IBD score was observed
Pairs	71	37MM, 26MF, 8FF	0	11
			1	37
			2	23
Trios	8	3MMM, 4MMF, 1FFM	2	5
			3	2
			4	1
Quartets	3	2MMMM, 1MMMF	4	2
			5	1
			6	–
Sextets	1	MMMMMM	8	1
			9	–
			10	–

IBD, identity by descent.
Green & Woodrow (1977) *T* statistic = 2.04; *P* < 0.05.

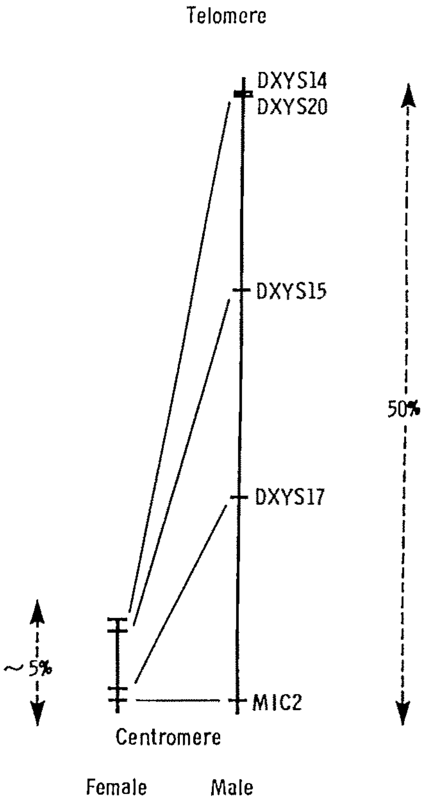

Fig. 1 Illustration of genetic distances separating the telomere and the sex-specific loci centromeric to the pseudo-autosomal boundary in male and female meiosis. DXYS14, 15, 17 and 20 are loci of known position on the genetic maps (Rouyer *et al*, 1986) and physical maps (Brown, 1988; Petit *et al*, 1988; Rappold & Lehrach, 1988). MIC2 is a gene close to the pseudo-autosomal boundary (Goodfellow *et al*, 1986). The recombination rates in female and male meiosis (5% and 50% respectively) determine the genetic distances.

Most recent studies (e.g. Angst *et al*, 1983; Gershon *et al*, 1988) suggest a genetic relationship between schizoaffective disorder and schizophrenia; it should be noted that erroneous inclusion of a non-related diagnostic category would weaken a finding of linkage. The sizes and sex ratios of the sibships are given in Table 1.

The DNA probe and Southern hybridisation

The probe p29C1, to the pseudo-autosomal telomeric locus DXYS14 (Fig. 1), detects hypervariable fragments on Southern blots prepared from EcoRI-digested DNA (Cooke *et al*, 1985) (Fig. 2). We have determined zygosity on more than 300 individuals at the locus and observed no homozygotes. The frequency of new mutations here has been estimated at 1% (unpublished observations). The frequency of homozygosity must therefore be extremely low. Consequently, both parents of an affected sib-pair will be uniquely heterozygous such that essentially all meioses are fully informative for linkage analysis. Similarly, it is usually possible to assign the parental origin of alleles in sibships even if DNA from only one parent is available. With such a probe an informative study can be carried out with a relatively modest number of affected sib-pairs and parents. Furthermore, because of the hypervariable nature of this locus, paternity can be confirmed at the same time (Cooke *et al*, 1985). Since the DXYS14 locus is not linked to sex (Fig. 1, and see Discussion) the findings with this probe can be analysed without regard to parental origin of illness genes or sex of ill sibling (see Discussion).

With informed consent, blood samples were taken from each subject and lymphoblastoid cell lines were established or DNA extracted directly. DNA was completely digested with an excess of EcoRI, size fractionated by electrophoresis through 0.7% agarose gels, transferred to Hybond-N-membranes (Amersham) using standard techniques and vacuum baked for 2 h at 80 °C. The probe p29C1 was labelled with ^{32}P using random hexanucleotide priming to a specific activity of $>10^8$ counts per minute per μg. Pre-hybridisation (4 h) and hybridisation (16 h) were in $3 \times SSPE$ ($1 \times SSPE =$ 0.18 mol/l NaCl, 10 mmol/l Na phosphate, pH 7.4, 1 mmol/l EDTA), non-fat milk powder (0.5%), sodium dodecyl sulphate (SDS) 1%, and denatured salmon sperm DNA (0.5 mg/ml) at 65 °C. Final washing stringency was $0.1 \times SSC$ (standard saline citrate), 0.1% SDS at 68 °C. Autoradiography was carried out at −70 °C for 16–48 h (Kodak XAR film backed with intensifying screens).

Autoradiographs were scored by four individuals (JC, RL, FO, MP) independently and disagreements were resolved by consensus. An additional restriction enzyme (TaqI) detecting variable fragments at the same genetic locus was used to confirm allele assignments in cases in which technical difficulties or lack of one parental sample made interpretation difficult. The method used was identical to that above.

Statistical analysis

The statistical method used is that of affected sib-pairs (Green & Woodrow, 1977). This relies on a calculation of the identity by descent (IBD) of each affected sib with respect to parental alleles at a particular locus, and takes into account sibships with more than two affected members. To make use of this technique both parents must be uniquely heterozygous (i.e. father's genotype 'AB', mother's 'CD') so that the parental origin of each allele in the affected sibling can be determined. The IBD method was designed for detecting linkage to the highly polymorphic human leucocyte antigen system, but can be used with other equally hypervariable DNA markers.

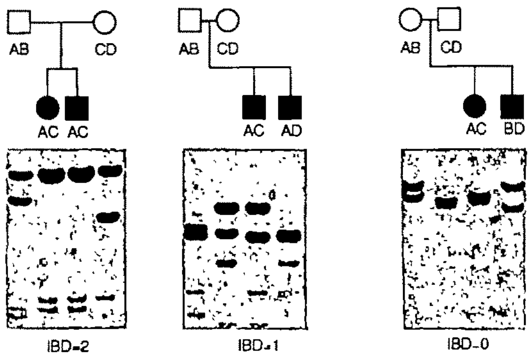

Fig. 2 Examples of affected sib-pairs with parents are shown to demonstrate the three possibilities with respect to identity-by-descent (IBD) scores, using the probe p29C1 for the DXYS14 locus with EcoRI digestion.

Assuming independent Mendelian assortment, offspring of genotypes AC, AD, BC and BD will occur with equal frequencies (i.e. each ¼). Therefore, sib-pairs allocated at random would be expected to share 2, 1, or 0 parental alleles with frequencies ¼ : ½ : ¼. If sib-pairs, selected on the basis that both are schizophrenic, are found to share alleles more often than expected by chance, this can be taken as evidence against the null hypothesis of independent assortment of marker and disease phenotype, that is, as evidence in favour of genetic linkage.

Data from multiple sibships are incorporated by counting the number of repeats of each allele (the number of times the presence of each allele exceeds one) represented within the sibship. Thus when an allele is inherited by x affected siblings, the score is $x-1$ repeats. The score for each of the four parental alleles is then summed for the affected siblings within each family. The possible total scores for families with more than two affected siblings are listed in Table 1. The distribution of repeats among all sibling sets is compared with what is expected from a random distribution of alleles where: $T=$ (total score $-$ 0.5 $-$ expected score) $\times$ expected variance. The T value is then compared with a standard normal integral table to obtain the appropriate significance level. It should be noted that the Green & Woodrow method is thought to be the most conservative with respect to information from multiple sibships (Suarez & van Eerdewegh, 1984).

Results

Identity-by-descent (IBD) scores (Fig. 2) for the 83 sibships are shown in Table 1. These results give a T statistic of 2.04; we were therefore able to reject the null hypothesis of independent assortment of alleles at $P<0.05$.

Since there is an excess of same-sex (particularly male) over opposite-sex sib-pairs (Table 1) in our sample, it is important (see Discussion) to use a probe to a locus that is not itself sex-linked. DXYS14 fulfils this criterion as far as can reasonably be ascertained by genetic linkage (Cooke *et al*, 1985) and physical mapping data (Petit *et al*, 1988). However, as a control, IBD scores were calculated for the 49 same-sex sib-pairs discordant for schizophrenia (i.e. schizophrenic or schizoaffective v. non-psychotic sibling). Since all these sib-pairs are of the same sex, if the above results were due to a bias arising from partial sex linkage, an even stronger skew towards IBD scores indicative of linkage would be expected. Fourteen pairs had an IBD score of 2, 21 an IBD of 1 and 14 an IBD of 0, suggesting that such a bias, if it exists, is minimal.

Because recombination within the region in male meiosis exceeds that in female meiosis by a factor of 10–20 (Rouyer *et al*, 1986), it would be predicted that with a

Table 2
Parental origin of alleles shared by affected siblings

Sibship size	Parental origin of alleles	
	maternal	paternal
Pairs ($n=71$)		
alleles shared (type AA or BB)	44	39
alleles not shared (type AB)	27	32
Triplets ($n=8$)		
all 3 siblings share an allele (type AAA or BBB)	2	2
only 2 siblings share an allele (type AAB or ABB)	6	6
Quartets ($n=3$)		
all 4 siblings share an allele (type AAAA or BBBB)	0	1
3 siblings share an allele (type AAAB or ABBB)	1	1
2 siblings share a parental allele (type AABB)	2	1
Sextets ($n=1$)		
3 siblings share a parental allele (type AAABBB)	1	1
χ^2	102.5	90.2
Degrees of freedom	83	83
P	0.07	0.28

The two alleles in the respective parents are designated A and B.

pseudo-autosomal disease locus the alleles that are shared by affected siblings will more frequently be of maternal than paternal origin. Analysis of parental origin (Table 2) indicates that of 71 pairs of siblings, a maternal allele is shared in 44 pairs while a paternal allele is shared in 39 pairs (by comparison with a chance expectation in each case of 35.5). When multiple sibships are taken into account (according to a formula developed by Dr I. D. Hill, Clinical Research Centre, Division of Medical Statistics) the excess of maternal alleles just fails to reach the 5% level of significance ($P=0.07$).

Discussion

These findings suggest there may be a locus for schizophrenia on the distal short arms of the X and Y chromosomes. Previous linkage studies in schizophrenia have focused on the q11–q13 region of chromosome 5 following the report of schizophrenia segregating with trisomy 5q11–q13 in two members of a family of Chinese origin (Bassett *et al*, 1988). A report of linkage of a dominant schizophrenia-susceptibility allele to markers p105–599Ha and p105–153Ra in five Icelandic and two English pedigrees (Sherrington *et al*, 1988) has not been confirmed either in a single large north Swedish pedigree (Kennedy *et al*, 1988) or in studies of 15 Scottish families (St Clair *et al*, 1989), of six Welsh families (McGuffin *et al*, 1990), a number of North American families (Aschauer *et al*, 1990; Crowe *et al*, 1990), nor in a subsample of the families in the present study (Kaufman *et al*, 1989). This suggests that a locus on chromosome 5, if it exists, can be related to no more than a small minority of cases of schizophrenia.

The segregation patterns of pseudo-autosomal loci indicate that X–Y recombination results from a single obligatory crossover in male meiosis in the pseudo-autosomal region, no double recombinational event having been observed in family analyses to date (Simmler *et al*, 1985; Cooke *et al*, 1985; Rouyer *et al*, 1986; Page *et al*, 1987). Consequently, there is a gradient of partial sex linkage along the pseudo-autosomal segment: telomeric loci (where 50% recombination takes place) show no sex linkage and therefore mimic autosomal inheritance (Burgoyne, 1982; Simmler *et al*, 1985; Rouyer *et al*, 1986); the tendency for an allele transmitted from an affected father to pass preferentially either to sons or to daughters (the characteristic of pseudo-autosomal transmission) will be maximal at the proximal pseudo-autosomal boundary; intermediate loci will give intermediate degrees of sex concordance in affected sibs.

Consistent with the hypothesis, in this sample there is an excess (mostly male–male) of same-sex siblings (Table 1). However, because of the gradient of sex linkage, pairs of siblings of the same sex will share alleles above chance expectation for any locus within the pseudo-autosomal region except at the telomere. For this reason we chose a probe to the telomeric locus DXYS14 for which an approximate 50% recombination fraction between DXYS14 and sex phenotype has been observed (Petit *et al*, 1988). This locus is therefore unlinked with sex, although it could be linked, as the findings suggest, to a more proximal putative disease locus, that itself shows partial sex linkage. The findings in the pairs of sibships concordant for sex but discordant for illness status confirm that sex linkage does *not* account for the excess of shared alleles in the affected sibships.

In theory, an assessment of the location of a pseudo-autosomal gene can be obtained from the size of the concordance-by-sex effect with paternal derivation of illness, but in practice such estimates have little precision (Crow *et al*, 1989, 1990). However, it is likely that the DXYS14 locus is still a considerable genetic distance in male meiosis from the putative disease locus (Fig. 1). This study can be followed by a two-point linkage analysis to attempt localisation of this locus in relation to the seven loci mapped to this region (Petit *et al*, 1988; Brown, 1988; Rappold & Lehrach, 1988), and to assess the proportion of schizophrenia attributable to this locus. However, for the reasons outlined, we feel that attempts at independent confirmation of these results should consider using the method of affected sib-pairs. Once subtelomeric probes are used in linkage analysis the problems raised by partial sex linkage and the radically differing recombination rates in male and female meiosis will need to be addressed.

Two genes, MIC2 (Goodfellow *et al*, 1986), and the granulocyte-macrophage colony stimulating factor receptor gene (Gough *et al*, 1990), but as yet no diseases, have been mapped to the pseudo-autosomal region, although Niikawa *et al* (1988) suggest that the Kabuki make-up (Niikawa-Kuroki) syndrome (characteristic dysmorphic features, mental retardation and post-natal growth deficiency) may be pseudo-autosomal dominant. The possibility of a susceptibility locus for schizophrenia in such a small and intensively mapped region of the genome could lead to the relatively early location of a psychosis gene.

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No Genetic Linkage Detected for Schizophrenia to Xq27–q28

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The hypothesis that at least a subgroup of familial cases of schizophrenia could be due to a genetic defect on the X chromosome is supported by the observation of an excess of X-chromosome aneuploidies (XXX and XXY) among populations of patients with psychosis. The distal long arm, Xq27–q28, is a candidate region where linkage has been claimed to manic–depressive disorder and a fragile site has been associated with schizophrenia spectrum disorders. The present study excluded linkage to a large part of this region using four polymorphic probes and multipoint lod-score analysis in 10 families with multiple members with schizophrenia.

Schizophrenia has generally not been considered to be linked to the X chromosome because of the frequency of male–male transmission, and the lack of sex linkage in segregation analyses of large samples of families with schizophrenic members. However, several reports suggest that examination of the X chromosome may be warranted in at least a subgroup of cases. These include the observations that sex-chromosome aneuploidies (specifically XXY and XXX) are increased among patients with schizophrenia, that pairs of relatives with schizophrenia are more apt to be of the same than opposite sex, and that relatives of females may be at a greater risk for development of illness than relatives of males (Crow, 1988; DeLisi & Crow, 1989).

The distal long arm of the X chromosome has been a likely candidate region since linkage to the G6PD and deutan colour-blindness loci within this region have been claimed for manic–depressive psychosis (Del Zompo *et al*, 1984; Mendlewicz *et al*, 1980, 1987; Baron *et al*, 1987). In addition, Reiss *et al* (1986, 1988) drew attention to a possible association of this region with schizophrenia when reporting the presence of schizophrenia spectrum diagnoses in female carriers of the fragile-X defect mapped to Xq27.3.

The presence of a fragile site in this region is thought to account for approximately 4–5% of all mental retardation in males (Rogers & Simensen, 1987; Webb *et al*, 1987) and 30–50% of X-linked male mental retardation. An excess of fragile X is also present among children with autism (Brown *et al*, 1986). The original case report of a syndrome with X-linked mental retardation (Martin & Bell, 1943) suggests that certain psychotic features may accompany the illness, and subsequent studies of family members found that psychotic illness and schizophrenia spectrum traits may be present in carriers of the defect (Fryns, 1984; Reiss *et al*, 1986, 1988).

Since there is some evidence of genetic overlap between schizophrenia and manic–depressive psychosis (Crow, 1986), the reported linkages, alone, provide evidence enough to pursue studies of this region of the X chromosome in schizophrenia, beginning with a focus on markers linked to the region of the fragile site. In a previous report (DeLisi *et al*, 1988), fragile sites were not detected in 46 random male schizophrenic patients; thus fragile X itself is unlikely to be associated with schizophrenia. We report here results using restriction fragment length polymorphisms (RFLPs) at four separate loci: (three distal and one proximal) all linked to the fragile site.

Method

We studied 20 families (9 from the USA, 11 from the UK) with at least two siblings having a diagnosis of chronic schizophrenia or schizoaffective disorder according to Research Diagnostic Criteria (RDC; Spitzer *et al*, 1977). These families were selected from a larger group of approximately 51 USA and 20 Northwick Park nuclear families who previously had blood samples taken for DNA analysis. Diagnoses of bipolar disorder, major depression and DSM–III schizotypal personality disorder (American Psychiatric Association, 1980) were occasionally present in other first-degree relatives in these families. Paternity was checked using probes for variable numbers of tandem repeats (VNTR). If the paternity in a family was suspect, that family was not used.

Families from the USA were recruited by advertisement throughout the country for families with at least two siblings ill with schizophrenia. A registry was established with the help of the National Alliance for Mental Illness, the Clinical Neurogenetics Branch of National Institute of Mental Health, and the Department of Psychiatry at SUNY Stony Brook, New York. Families from the UK were identified from a north-west London catchment area and were families of index patients treated at Northwick Park Hospital, some of whom had participated in research clinical trials at the Clinical Research Centre. Psychiatric interviews were performed using a modified version of the Schedule for Affective Disorders and Schizophrenia, Lifetime version (SADS–L; Spitzer & Endicott, 1978; E. Gershon, NIMH, unpublished) for the USA sample, and the Present State Examination (PSE; Wing *et al*, 1974) for the UK sample. Diagnoses were made based on interviews, treatment records, and information obtained from family members and treating clinicians using the RDC. DeLisi *et al* (1987) and Crow *et al* (1989) give further clinical details. Although structured interview schedules used to gather clinical information were different in the two independent sources of families, similar information was obtained, and the diagnoses were made using the same criteria in both locations. Diagnostic reliability had previously been established between diagnosers (LED and TJC).

Families for the present studies were selected if they appeared to have maternal inheritance of psychosis by family history, or consisted of multiple ill male siblings. Since male offspring must receive their X chromosome from their mother, linkage could easily be recognised if ill male siblings share the same maternal alleles. Since daughters must inherit the father's one X chromosome, father–daughter in contrast to maternal transmission is not informative for linkage studies. Although we attempted to eliminate families with father–son transmission of illness, reliable diagnostic information often was not available for preceding generations in these families, and we do not know the relationship of other psychiatric disorders (e.g. major depression) to the inheritance of schizophrenia. Thus, male–male transmission of illness (which is inconsistent with X-chromosome linkage) could not be entirely ruled out. These families were not necessarily strong candidates for X-linked illness. Rather, they were chosen as the ones present in a large sample of families that would be the most likely to be X-linked.

The DNA was isolated from cultured lymphoblasts and digested with restriction endonucleases, TaqI, PstI, and BclI in separate aliquots. DNA fragments were resolved on 0.7% agarose gels and transferred to nylon membranes using 0.025 mol/l $NaPO_4$, pH 6.6. Filters were hybridised with probes 55E, 1A1, St-14, and F8C, representing the genetic loci DXS105, DXS374, DXS52, and F8C, respectively. The presumed gene order of these loci is shown in Fig. 1 (Mandel *et al*, 1989). TaqI identifies St-14 RFLPs, PstI, 55E and BclI, F8C. Probes were purified from the plasma vector sequences by restriction digestion with the appropriate enzymes, agarose gel electrophoresis, electroelution, and radiolabelled with ^{32}P using standard methods (Maniatis *et al*, 1982). RFLPs identified by each probe and their corresponding allele symbols are listed in Table 1. Autoradiographs of the resultant blots were scored and alleles assigned without knowledge of the affected status of each individual.

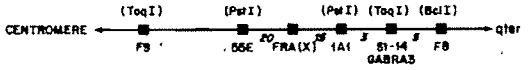

Fig. 1 Distal long arm of the X chromosome: map of gene order and distances in centimorgans (italic) between loci for probes used in the present studies.

Table 1
Probes, corresponding enzymes used to identify RFLPs, and bands for each allele assignment

Alleles	Bands (kb)
St-14 (TaqI)	
A_1	6.6
A_2	5.4, 5.2
A_3	5.8
A_4	4.5
A_5	4.1
A_6	4.0
A_{7a}	3.9
A_{7b}	3.6
A_8	3.4
A_9	1.9
A_{10}	14.0
Factor 8 (BclI)	
B_1	0.9
B_2	1.2
55E (PstI)	
E	16
e	10
1A1 (PstI)	
Q	5.2
q	2.9, 2.3

Multipoint linkage analysis was performed using the LINKMAP program, version 5.03 (Lathrop *et al*, 1984; Ott, 1985). For this analysis, we assumed the gene frequencies of each allele at each marker to be equal in lieu of more accurate information. Marker order and intermarker distances were fixed as follows: 55E–1A1, 35cM; 1A1–St-14, 3cM; St-14–F8, 5cM (Fig. 1). At the disease locus, an X-linked dominant gene with penetrance of 0.30 and 0.60 and gene frequency of 0.01 was assumed. One low-penetrance and one high-penetrance value for schizophrenia was used since this parameter is uncertain. The families were then analysed using two diagnostic boundaries. Firstly, we used a limited diagnostic model in which only people with diagnoses of chronic schizophrenia or chronic schizoaffective disorder were taken to be affected, while those with bipolar or unipolar affective disorder or schizotypal personality disorders were taken to be of unknown disease phenotype. Secondly, we analysed the families under a broad diagnostic system, considering all of the above disorders as variants of the same gene. Four-point linkage analyses were then performed, moving the disease position along a fixed map of marker loci.

Results

Of the 20 families screened, 10 were informative for at least one of the probes (i.e. the mother was heterozygous relative to the father). Figure 2 is an illustration of the 10 informative pedigrees and indicates the alleles present for each individual at each typed locus. The disease is considered

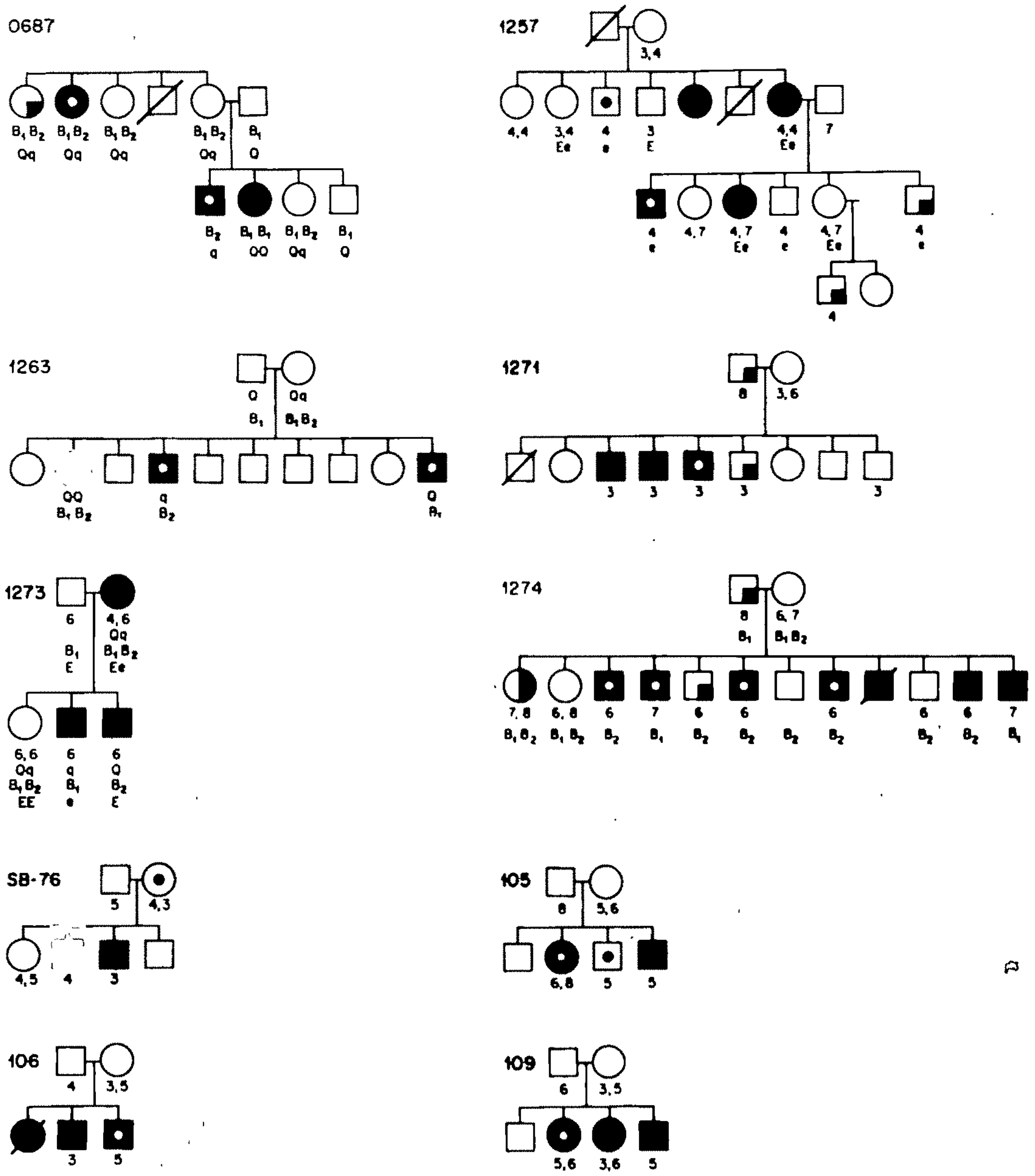

Fig. 2 Ten pedigrees and the alleles for each individual studied (□ male, ○ female, bar indicates deceased; ■ schizophrenia; ▣ schizoaffective disorder (schizophrenic type), ◲ major depression, ◨ bipolar I, ⊡ schizotypal personality; same respective diagnoses in females). Families 0687, 1257, and 1273 were selected for maternal inheritance as indicated. Family 1263 was selected because three ill siblings were available; no close relatives were known to have psychosis; however, on further inquiry three paternal distal relatives were noted to have affective disorder and possible psychosis. Although family 1271 had a paternal history of major depression without hospital admission in the father and grandmother, no psychosis was noted on either side. Family 1274 was selected because of the unusually high number of ill males, although psychosis was present in third-degree relatives on both maternal and paternal sides of the family. Family SB-76 has evidence of schizotypal personality disorder in the mother; history of illness on the paternal side is unknown. Families 106 and 109 have no known history of psychosis on either parental side. Family 105 has a maternal uncle and grandmother with psychosis. Alleles for each locus are illustrated only if they were informative.

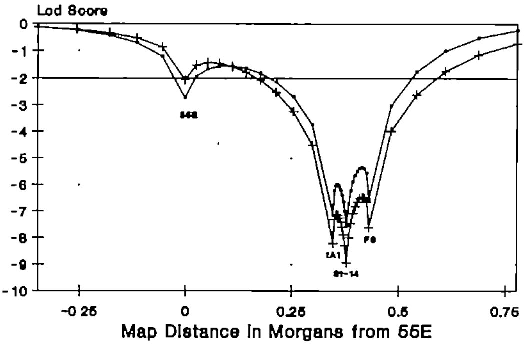

Fig. 3 Multipoint lod-score analyses for all families together using broad (■-■ and narrow (++) diagnostic criteria and 30% penetrance.

to be excluded from all points in Fig. 3 where the lod score is less than −2, by the conventional criterion. In this case, under both diagnostic criteria, tight linkage of the disease to the markers 1A1, St-14, and F8C is ruled out with a high degree of certainty, while the region near 55E is less clear. Although it is unlikely that the disease is in this region since the lod score never approaches a positive level, more families may be needed to exclude this distance proximal to the fragile site.

Two-point lod scores were also calculated for the disease and each locus separately. Each of these comparisons was considered not significant since not all the families were informative for each allele. A penetrance of 30% was assumed for the analysis shown in Fig. 3. As can be seen in Fig. 2, two families (1257 and 1271) have ill siblings who all share the same alleles, although these families also have well siblings with those alleles. If the penetrance is set low, the unaffected relatives contribute little to the lod-score analyses, and this would maximise the likelihood of obtaining a positive score; despite this, the overall lod scores were still negative. Calculations were also performed using a penetrance of 60% with almost identical exclusionary lod scores obtained.

The lod scores for each family were also analysed using the HOMOG program of Ott (1985), and no statistical evidence for heterogeneity was found in these families under any of the models considered. However, the use of HOMOG in this sample cannot refute homogeneity of non-linkage.

Discussion

Data from the present study fail to support linkage of schizophrenia or schizoaffective disorder to a region within Xq27–28, close to the fragile site. Thus, although schizophrenia, schizoaffective disorder and affective psychoses seem to overlap in families, our data in families with predominantly schizophrenic psychoses are not consistent with previously reported linkages of bipolar disorder to this region (Del Zompo *et al*, 1984; Mendlewicz *et al*, 1980; Baron *et al*, 1987). These positive reports could have been chance findings that may not represent a true genetic linkage, or could account for psychosis in a small proportion of families that, owing to their rarity, we failed to identify in our sample. In addition, we could have failed to select families that were appropriate for this study. While the pattern of transmission within these nuclear families appeared consistent with X linkage, a history of atypical illness or affective disorder in other relatives in some instances suggested inconsistency with an X-linked pattern of inheritance (as might be the case with family 1263). In fact, clear mother–son transmission, the form of transmission expected to be most common in X-linked inheritance, was not prevalent in our sample as a whole (approximately 27% maternal inheritance, of which only 7.5% were all male ill offspring – see Crow *et al* (1989)). It is also possible that the present report focused on a diagnostic category of psychosis that is genetically distinct from the inherited affective disorders of the previous reports.

There is still reason, however, to suspect that the X chromosome is involved in the development of psychosis, and other regions of the X chromosome continue to be of interest. One possibility is that the locus is pseudo-autosomal, within that portion of the short arm of the X and Y chromosomes with complete sequence homology and obligatory recombination in male meiosis. The occurrence of a gene for psychosis within this region has been proposed (Crow, 1988), and given some support in a study that showed a tendency towards same-sex concordance for illness with paternal, but not maternal, origin (Crow *et al*, 1989) and more directly by linkage analysis in sib-pairs using a highly polymorphic telomeric probe in the distal pseudo-autosomal region (Collinge *et al*, 1989, and previous paper, this issue).

Although further investigation of the Xq region close to the factor IX locus may be needed, given the present data, examination of the more distal Xq region linked to the fragile site is unlikely to be worth further pursuit in families with schizophrenia or schizoaffective psychosis. Although there are unusual case reports of an association of other disease alleles in this region (i.e. G6PD, the fragile-X chromosome, and colour blindness) with psychosis, it is unlikely that these positive linkages to this region could generalise to a substantial proportion of schizophrenic cases.

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No Evidence for a Susceptibility Locus Predisposing to Manic Depression in the Region of the Dopamine (D2) Receptor Gene

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Recent reports of cytogenetic abnormalities linked to psychiatric illness and the localisations of the genes for the dopamine (D2) receptor and tyrosinase on the long arm of chromosome 11 have suggested that susceptibility loci for schizophrenia and manic depression might be situated in this region. We could find no evidence for linkage in five Icelandic pedigrees between manic depression and markers in this region, and we have excluded candidate genes coding for the D2 receptor and tyrosinase. We conclude that mutations at loci in this region are not a common cause of manic depression in the population studied.

Two recent reports have focused interest on the long arm of chromosome 11 in the genetic susceptibility to manic depression because of associations between cytogenetic abnormalities and affective disorder. Smith *et al* (1989) described an American pedigree containing five members suffering from bipolar affective disorder, all of whom had a translocation from chromosome 11 to chromosome 9 ((9;11)t (pter;q22.3)). In a report by St Clair *et al* (1990) a Scottish family was described in which several individuals had developed schizophrenia, schizoaffective illness and other psychiatric illnesses and also had a translocation from chromosome 11 (11q25) to chromosome 1. The evidence for this not being a chance association was quite strong because the lod score (log of odds ratio) for linkage between psychiatric illness and the translocation is above 4 at zero recombination, although this was dependent on which diagnoses were used to indicate affection. (Conventionally a lod score of 3 or above is taken to be strongly suggestive of linkage, and is considered unlikely to occur by chance.)

The existence of two independent pedigrees each multiply affected with psychotic illness apparently linked to two translocations involving one region of chromosome 11 suggests that mutations in genes at this site may predispose to psychiatric illness. Reports of such cytogenic abnormalities can often provide a fruitful pointer for subsequent linkage studies, a classic example being the report by Bassett *et al* (1988) of a partial trisomy of chromosome 5 cosegregating with schizophrenia which led to a report of positive linkage to the same region by Sherrington *et al* (1988). In the present instance there are also *a priori* grounds for interest in the long arm of chromosome 11 because of the localisation there of the D2 receptor and tyrosinase genes. Mutations in these genes could be predisposing to psychiatric illness. The gene for the type-2 dopamine receptor has been localised to 11q22.3–q23 (Grandy *et al*, 1989). Disturbances of dopamine transmission have often been thought to be a possible factor in the genesis of psychotic illness, and both schizophrenia and the manic phase of manic depression respond to dopamine receptor antagonists. A less convincing, though still interesting, candidate gene for schizophrenia and schizoaffective disorder is the gene for tyrosinase. Although tyrosinase is not thought to be directly involved in the metabolic pathways for the synthesis or degradation of centrally acting neurotransmitters, there have been reports of families in which schizophrenia cosegregates with tyrosinase-negative albinism (Baron, 1976; Clarke & Buckley, 1989). The gene for tyrosinase has been localised to 11q21.4 (Spritz *et al*, 1989). The existence of two genes of interest in a region where cytogenetic abnormalities were linked to psychotic illness led us to search for evidence of linkage in our own sample of multiply affected pedigrees.

Method

We examined five Icelandic kindreds containing multiple cases of the unipolar and bipolar forms of manic depression (Fig. 1). Psychiatric diagnoses were assigned using Research Diagnostic Criteria (RDC; Spitzer *et al*, 1978). Subjects were interviewed by a psychiatrist, who was blind to genotyping, using the Schedule for Affective Disorders and Schizophrenia, Lifetime version (SADS–L; Spitzer & Endicott, 1977). This information was supplemented by material from case notes. Extensive tracing of pedigrees was carried out to ascertain as far as possible the diagnoses of other members of the kindreds. Care was taken to exclude pedigrees containing schizophrenic cases and those pedigrees which did not have a unilateral source of manic depression. Two levels of diagnosis were used in subsequent analyses to designate individuals as affected. For the first level only

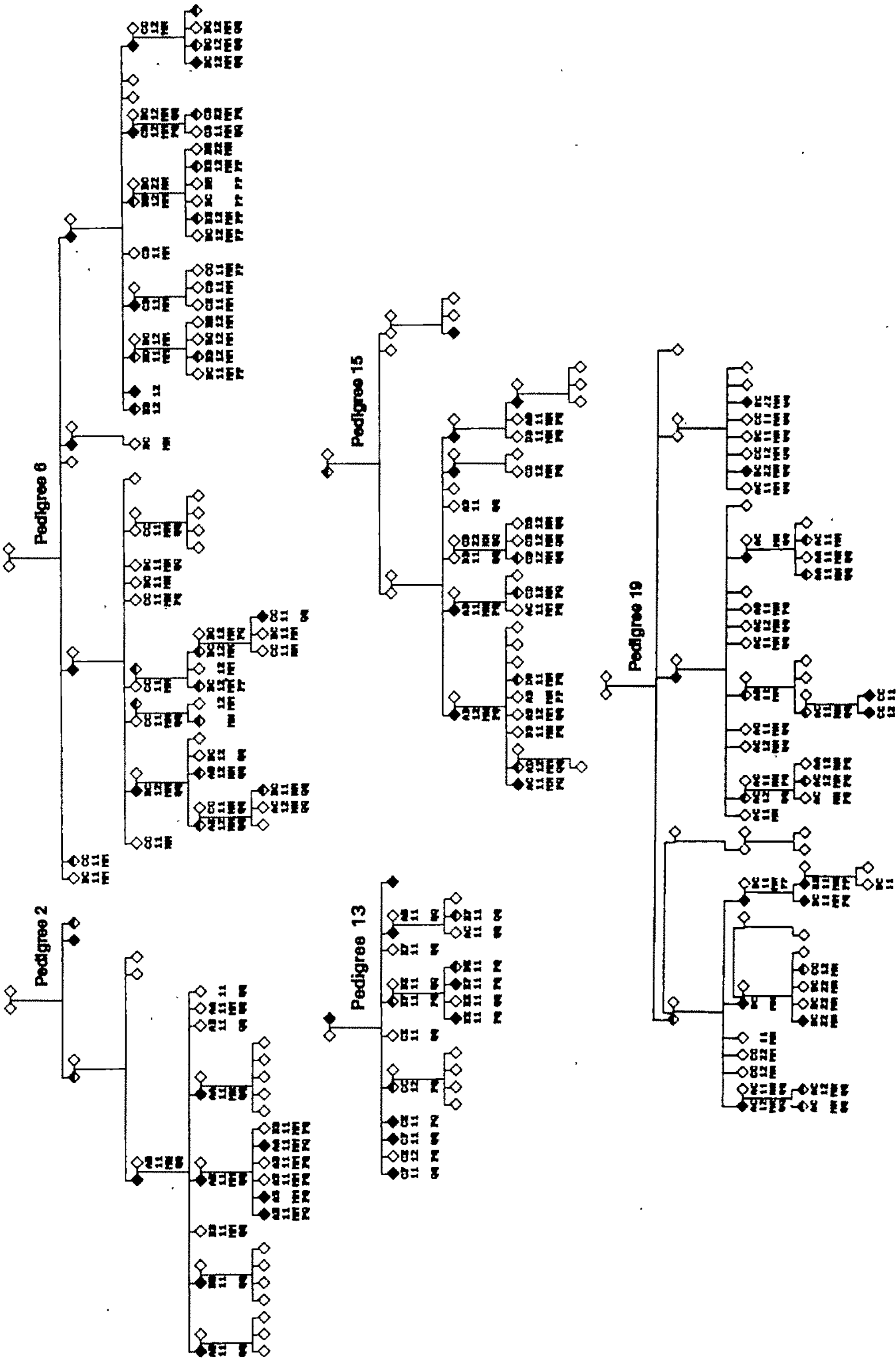

Fig. 1 The five pedigrees examined for linkage of manic depression to the genes for the D2 receptor. ◆ Bipolar I or II, ◈ major or minor depressive disorder (in absence of drug or alcohol abuse). The genotypes examined are coded under each individual: A–E, pMS51; 1 2, phi 2–14; M N, phi 6–3; P Q, phi HD2G1.

those individuals who had fulfilled the criteria for either mania or hypomania (bipolar I and bipolar II) were classed as affected. The second level included as affected all those individuals suffering from mania, hypomania, or major or minor depressive disorder, or intermittent depressive disorder, but excluding those with unipolar depression combined with drug or alcohol abuse. (There were only seven additional individuals who would have qualified as affected had the last criterion not been applied.) Three of the pedigrees (2, 6 and 13) had been studied previously for linkage between manic depression and the HRAS, tyrosine hydroxylase and insulin loci on 11p with negative results (Hodgkinson *et al*, 1987*a*), and had also been investigated with hypervariable 'minisatellite' markers (Hodgkinson *et al*, 1987*b*).

Affective illness in the pedigrees appeared to segregate as an autosomal-dominant disease with incomplete penetrance, although the effects of selection bias make it impossible to be definitive on this point. A segregation analysis carried out with the computer program POINTER (Lalouel *et al*, 1983) was consistent with an autosomal-dominant mode of inheritance and provided maximum-likelihood estimates of heterozygote penetrance of 0.7 for all affective illness and 0.4 for bipolar illness. These parameters were used in subsequent linkage analysis, with the unaffected homozygote penetrance being set to 0.01 for bipolar and unipolar affective disorder and 0.001 for bipolar illness. These values were chosen so that phenocopies and errors in diagnosis would not unduly distort the results obtained by linkage analysis. The affection rate was essentially equal in males and females, and there was no appreciable difference in affection rate between different age groups (all the subjects were aged 20 years or over). The subjects were therefore not divided into different liability classes and the same penetrance parameters were used for all subjects. Diagnoses are shown in the pedigree diagrams according to the key (Fig. 1). The sex of individuals has been concealed to maintain confidentiality.

To identify genetic polymorphisms, probes pMS51, phi 6–3, phi 2–14 and phi HD2G1 were used to detect DNA fragments at loci D11S97, D11S85, D11S36 and DRD2 respectively (Wong *et al*, 1987; Maslen *et al*, 1988; Grandy *et al*, 1989). Phi HD2G1 is a subclone of the D2 receptor gene. DNA was digested with HaeIII, MspI, RsaI and TaqI restriction enzymes and was separated by size in 0.8% agarose gels and transferred by Southern blotting to nylon filters according to standard techniques. Probes pMS51, phi 6–3, phi 2–14 and phi HD2G1 were labelled with P^{32} and hybridised to the respective filters. Probe phi 2–14 hybridises to two allelic fragments that are 2.95 kB and 2.1 kB (shown as 1 and 2 in Fig. 1) with allele frequencies of 0.62 and 0.38. Probe phi 6–3 hybridises to two allelic fragments that are 9.5 kB and 3.85 kB (shown as M and N in Fig. 1) with allele frequencies of 0.43 and 0.57. Phi HD2G1 detects two allelic fragments of 6.6 kB and 3.7 + 2.9 kB with allele frequencies of 0.24 and 0.76 (shown as P and Q in Fig. 1). pMS51 hybridises to a variable number of tandem repeats (VNTR) with many alleles in these families. These were rationalised to five alleles for the purpose of linkage analysis without loss of information, and the allele frequencies were all set to 0.2

Linkage analysis was performed using the MLINK and LINKMAP computer programs from LINKAGE (Lathrop *et al*, 1985). Two-point lod scores were calculated between affection status and marker data for each disease model. Four-point maps were generated for each disease model against phi HD2G1, phi 6–3 and pMS51. For multipoint linkage analysis the female : male recombination ratio was set to 1.5.

In order to investigate the sensitivity of the results obtained to changes in the parameters of the genetic model specified, all the two-point lod scores were recalculated using a selection of different values for these parameters. For the bipolar disease model, lod scores were calculated for penetrances of 0.4, 0.65 and 0.9 assuming dominant transmission and for penetrances of 0.7 and 0.9 assuming recessive transmission. For the model including unipolar and bipolar affective disorder, lod scores were calculated with penetrances set to 0.7 and 0.9 for both dominant and recessive transmission. For both models the analyses for recessive transmission were repeated with the disease gene frequency set to a higher value of 0.1. Finally, all the analyses for the second disease model were repeated with the normal homozygote penetrance set to 0.05 instead of 0.01. Since all these analyses were performed for each

Table 1
Two-point lod scores between disease and marker loci, totalled over all five families

	Recombination frequency							
	0.000	0.001	0.010	0.050	0.100	0.200	0.300	0.400
Phi 2–14								
all cases	−6.661	−6.474	−5.281	−2.901	−1.628	−0.457	−0.038	0.020
bipolar	−0.998	−0.978	−0.798	−0.239	0.084	0.278	0.227	0.095
Phi 6–3								
all cases	−5.639	−5.464	−4.416	−2.551	−1.571	−0.659	−0.252	−0.064
bipolar	−1.881	−1.863	−1.716	−1.262	−0.902	−0.464	−0.215	−0.073
pMS51								
all cases	−14.709	−14.484	−12.789	−8.723	−5.907	−2.775	−1.202	−0.424
bipolar	−5.903	−5.586	−4.200	−2.097	−1.073	−0.310	−0.127	−0.093
Phi HD2G1								
all cases	−4.840	−4.806	−4.373	−2.910	−1.869	−0.713	−0.200	−0.020
bipolar	−2.114	−2.077	−1.834	−1.230	−0.773	−0.301	−0.099	−0.023

Table 2

Four-point map of lod scores for affective illness against pMS51, phi 6–3 and phi HD2G1

Pedigree	Distance in centimorgans (male)															
	−21.182	−10.137	0.000[1]	4.009	8.069	12.239	16.582	21.182[2]	25.191	29.252	33.421	37.765	42.365[3]	52.502	63.547	77.022
2	−0.088	−0.203	−0.484	−0.342	−0.253	−0.196	−0.161	−0.146	−0.120	−0.097	−0.077	−0.060	−0.045	−0.027	−0.014	−0.005
6	−0.273	−0.774	−3.059	−1.677	−1.258	−1.122	−1.259	−2.640	−1.617	−1.407	−1.434	−1.775	−3.119	−0.961	−0.406	−0.163
13	−0.319	−0.869	−2.073	−1.442	−0.879	−0.508	−0.275	−0.148	−0.124	−0.151	−0.256	−0.467	−0.602	−0.185	0.117	0.136
15	−0.213	−0.571	−2.318	−1.363	−1.054	−0.940	−0.985	−1.385	−0.975	−0.779	−0.672	−0.629	−0.661	−0.244	−0.075	−0.016
19	−1.047	−2.228	−6.325	−3.509	−2.469	−1.850	−1.520	−2.675	−1.493	−1.418	−1.538	−1.864	−2.940	−1.406	−0.728	−0.331
Total	−1.939	−4.645	−14.260	−8.332	−5.913	−4.615	−4.201	−6.994	−4.329	−3.861	−3.976	−4.795	−7.367	−2.824	−1.105	−0.378

1. Location of pMS51.
2. Location of phi 6–3.
3. Location of phi HD2G1.

Table 3

Four-point map of lod scores for bipolar illness against pMS51, phi 6–3 and phi HD2G1

Pedigree	Distance in centimorgans (male)															
	−21.182	−10.137	0.000[1]	4.009	8.069	12.239	16.582	21.182[2]	25.191	29.252	33.421	37.765	42.365[3]	52.502	63.547	77.022
2	−0.131	−0.321	−1.232	−0.605	−0.394	−0.278	−0.205	−0.159	−0.129	−0.104	−0.082	−0.063	−0.047	−0.028	−0.014	−0.006
6	0.064	0.043	−1.468	−0.151	−0.065	−0.129	−0.314	−0.812	−0.500	−0.307	−0.171	−0.058	0.060	−0.018	−0.041	−0.037
13	−0.081	−0.263	−0.880	−0.574	−0.305	−0.165	−0.105	−0.105	−0.136	−0.202	−0.331	−0.594	−1.028	−0.337	−0.063	0.006
15	0.001	0.003	−0.004	0.027	0.056	0.087	0.119	0.153	0.175	0.200	0.229	0.266	0.311	0.227	0.135	0.055
19	−0.373	−0.610	−2.490	−1.080	−0.797	−0.743	−0.850	−1.367	−1.170	−1.129	−1.194	−1.393	−2.032	−0.861	−0.446	−0.215
Total	−0.519	−1.148	−6.073	−2.384	−1.505	−1.228	−1.355	−2.291	−1.761	−1.542	−1.548	−1.841	−2.736	−1.018	−0.429	−0.196

1. Location of pMS51.
2. Location of phi 6–3.
3. Location of HD2G1.

of the four markers, a total of 76 two-point lod-score tables were calculated.

Results

The two-point analyses excluded close linkage between affective illness and each of the marker loci (Table 1). Two-point analyses also excluded close linkage between bipolar illness alone and D11S97 or DRD2. Multipoint analysis excluded linkage at lod score of −2.00 or less between affective illness and the entire region between D11S97 and DRD2 together with a region of at least 10 centimorgans (cM) on either side (Table 2, Fig. 2). Taking bipolar cases only as affected produced a less complete exclusion (Table 3), but there was nevertheless no evidence in favour of linkage. The inclusion of the seven individuals with drug or alcohol abuse as well as unipolar depression as cases did not produce results which were materially different from those obtained when they were excluded.

When the parameters of the genetic model were altered, increasing the abnormal homozygote and heterozygote penetrance led to lod scores which were more negative in all cases. Increasing the normal homozygote penetrance for affective illness from 0.01 to 0.05 produced slightly less negative lod scores. Specifying recessive transmission for the bipolar model led to lod scores which were in some cases slightly less negative than for dominant transmission. However, the lod scores became markedly less negative if recessive transmission was specified and all cases of affective illness were included, particularly if the higher normal homozygote penetrance value of 0.05 was used. Overall, there was no suggestion that the disease locus might be linked to any of the markers and the lod scores remained negative with all markers at all recombination fractions. The magnitude of these lod scores was dependent on whether or not unipolar cases were included as affected, whether dominant or recessive transmission was specified, and on the difference between the normal and abnormal homozygote penetrances.

Discussion

Linkage between a disease locus and a genetic marker will only be detected if an appropriate mode of transmission is specified for the disease, otherwise false-negative results may occur. Conversely, to exclude linkage confidently it is necessary to show that sufficiently negative lod scores are obtained for all plausible genetic models. Although we did our best to select an appropriate model by first performing a segregation analysis on our pedigrees, it is possible that the selection bias involved in recruiting pedigrees for linkage rendered the parameters obtained inaccurate. For this reason the two-point analyses were repeated using a wide selection of other parameters. The lod scores remained convincingly negative in all cases except when recessive transmission was specified and both bipolar and unipolar cases were classed as affected. However, a recessive mode of transmission does not seem plausible given the low population prevalence of bipolar disorder together with the high rate observed in these pedigrees, and also the apparently dominant effect of the cytogenetic abnormality in the pedigree described by Smith *et al* (1989). On balance we would therefore claim that our results provide a fairly convincing exclusion of the region studied which is not critically dependent on unjustified assumptions concerning the mode of transmission.

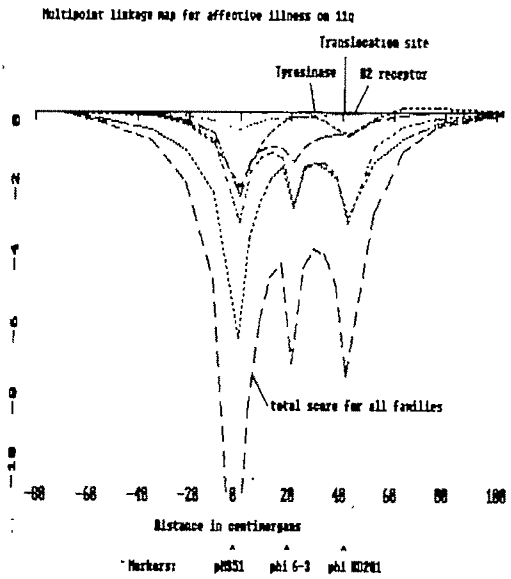

Fig. 2 Multipoint linkage map for affective illness on 11q.

Since the region of exclusion encompasses the genes for the D2 receptor and tyrosinase we conclude that abnormalities of these genes are unlikely to be the cause of the bipolar and unipolar affective illnesses occurring in these families. The site of the reported translocations is also excluded as containing a susceptibility locus in these families. If it is accepted that the multiple cases of psychotic mental illness occurring in the American and Scottish pedigrees are due to an abnormality at this site then this implies that there is genetic heterogeneity between these and the Icelandic pedigrees. There is already evidence in favour of heterogeneity for both manic depression and schizophrenia. There have been repeated reports of X-linked manic depression occurring in some pedigrees (Winokur *et al*, 1969; Del Zompo *et al*, 1984; Mendlewicz & Fleiss, 1974; Baron, 1977; Mendlewicz *et al*, 1980, 1987; Baron *et al*, 1987), yet it has been demonstrated that not all cases are X-linked (Hodgkinson *et al*, 1987*a*; Detera-Wadleigh *et al*, 1987; Holmes *et al*, 1989; Berrettini *et al*, 1990). There has also been a previous report of autosomal linkage to a locus on chromosome 11p (Egeland *et al*, 1987) but this has been questioned (Kelsoe *et al*, 1989). With schizophrenia there have been reports of linkage to a locus on chromosome 5 (Bassett *et al*, 1988; Sherrington *et al*, 1988), but other pedigrees have been reported as excluding linkage to this locus (Kennedy *et al*, 1988; St Clair *et al*, 1989).

It is possible that differences in gene frequencies distributed geographically between the samples may in part explain the failure to detect linkage in a significant proportion of the Icelandic families, and it may be that 11q-linked psychotic illness is quite common in other areas. On the other hand, the two pedigrees previously reported may be quite unrepresentative and abnormalities at this site may be only rarely associated with mental illness, or the associations may have occurred by chance. Further linkage studies will eventually resolve the question. It seems that genetic linkage research into common disorders such as bipolar and unipolar affective illness will necessarily have to allow for the strong probability of non-allelic heterogeneity of linkage.

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Changes in Patient Coping Style Following Individual and Family Treatment for Schizophrenia

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Changes in relatives' affective attitudes are important contributors to the impact of family psychoeducational programmes on the course of schizophrenia. It remains unclear whether similar changes occur in the interactional style of schizophrenic patients participating in psychoeducational treatment. This study examined changes in the interactional style (coping style) of 33 schizophrenic patients in individual or family treatment. Significant changes were seen in the interactional style of the patients participating in the individual treatment. Similar changes were evident, but not significant, in the family treatment group. The quality of patient interactional style before or after treatment did not predict relapse in either group. Changes in relatives' interactional style early in family treatment are necessary to affect the short-term course of schizophrenia. Modification in patient behaviour during the early phase does not have similar predictive value.

Numerous studies have suggested that affective attitudes expressed by close relatives of a schizophrenic patient are predictive of recurrence of the disorder (Brown *et al*, 1962, 1972; Vaughn & Leff, 1976*a*; Vaughn *et al*, 1984; Nuechterlein *et al*, 1986; Karno *et al*, 1987). These investigations were spearheaded by the development of a measure of the affective milieu of the family, expressed emotion (EE). A rating of EE is obtained through a semi-structured interview with relatives, the Camberwell Family Interview (CFI; Vaughn & Leff, 1976*b*). The studies found that family environments with high EE were associated with greater rates of relapse than families with low EE.

These studies of EE stimulated the development of family-focused interventions, designed to modify the attributes of intrafamilial relationships believed to increase the risk of relapse. Five controlled trials have reported substantial reductions in relapse when family therapy was added to maintenance drug treatment (Goldstein *et al*, 1978; Leff *et al*, 1982; Falloon *et al*, 1982, 1985; Hogarty *et al*, 1986; Tarrier *et al*, 1988). Further analyses have examined whether psychoeducational family therapy has achieved these effects by altering those negative aspects of family interaction specified by the EE literature: criticism and over-involvement. In studies in which the CFI was repeated after treatment, psychoeducational family treatment was associated with a reduction in EE status of the family, while drug treatment alone was not (Hogarty *et al*, 1986; Tarrier *et al*, 1988; Leff *et al*, 1989).

These studies of EE only measured whether *attitudes* expressed during an interview with a relative were modified, but not whether the family's actual interactional or behavioural patterns changed. Doane *et al* (1985, 1986), working within the Falloon treatment project, went a step further and measured changes in the relatives' affective style (AS), which is considered an interactional analogue of the EE construct. AS was assessed before therapy and after three months of the nine-month treatment programme. Negative AS was reduced in the family-plus-drug treatment condition as contrasted with the individual-plus-medication condition. Further, the degree to which negative AS was reduced at three months predicted both the likelihood of a major exacerbation of symptoms and the social functioning of the patient at nine-month follow-up.

These investigations of the therapeutic process have supported the hypothesis that changes in the relatives' affective attitudes and/or behaviour are important measures of the efficacy of these psychoeducational programmes. Interestingly, no one has examined the impact of these treatment programmes on the patient's interactional style with relatives following assignment to either treatment. Thus, we do not know if there are changes in the interactional style of the schizophrenic patients assigned to psychoeducational family therapy or if these changes are necessary or significant contributors to relapse prevention.

The present paper addresses the neglected issue of whether a programme of behavioural family therapy does, in fact, modify the patient's mode of interacting with key relatives and thereby plays some role in relapse prevention. We utilised the same systematically collected family interaction data assessed by Doane *et al* (1985, 1986) from the Falloon treatment study (Falloon *et al*, 1984) but focused instead on the patient's interactional behaviour before and after treatment. These analyses use the recently developed Patient Coping Style (CS) coding system (Goldstein *et al*, 1989; Strachan *et al*, 1989) which assesses the manner in which patients deal with relatives during directly observed family interactions. Previous studies (Goldstein *et al*, 1989; Strachan *et al*, 1989) found that the CS coding system was sensitive to the different ways patients behaved with high-EE and low-EE relatives and, therefore, this seemed appropriate for analysing the impact of family treatment on the interactional style of schizophrenic patients.

Method

The subjects were 33 schizophrenic patients and one or both of their biological parents. The patients had a classification of schizophrenia on the Present State Examination CATEGO criteria (Wing *et al*, 1974) and met DSM-III (American Psychiatric Association, 1980) criteria for schizophrenia. The patients were recruited for a treatment study at the University of Southern California comparing individual and family therapy of schizophrenia. Subjects were between 18 and 41 years of age, had English as their primary language, and resided, or had daily contact with, one or both biological parents.

The patient sample consisted of 11 women and 22 men (mean age 26.1 years, s.d. 6.04). Approximately half of the patients were from dual-parent and half from single-parent families. Fifteen were Caucasian, 11 were African-American, six were Mexican-American, and one was Asian. The socioeconomic status of the patients was middle to lower-middle class, based on Hollingshead-Redlich (Hollingshead & Redlich, 1958) criteria (mean 3.66, s.d. 1.7, data unavailable for one patient) and their mean years of education was 13 (s.d. 1.81, data only available for 32 patients). The illness history of the patient sample was as follows: mean number of psychiatric admissions was 3.64 (s.d. 2.37), mean number of total months in hospital was 3.56 (s.d. 4.77, data unavailable for one patient) and mean age of onset of psychosis was 21.9 (s.d. 5.48, data from 32 patients).

A total of 39 patients were initially recruited for the study and informed consent was obtained from the patients and their family members. Eighteen were randomly assigned to the family treatment, 18 to individual treatment. At the time of the post-therapy assessment one patient in the individual treatment was not available, another patient's family assessment interaction task could not be scored, and a third patient had different family members attend the post-therapy assessment. Thus, data analyses are from a total of 33 patients.

Treatment conditions

Therapy protocols began following discharge and a subsequent four to six weeks of clinical stabilisation. Both therapies consisted of weekly sessions for three months and biweekly sessions for the next six months. The patients were followed for two years after starting their assigned treatment. The individual treatment consisted of a clinic-based supportive psychotherapy which involved case management, optimal maintenance of medication, crisis intervention when necessary, and education concerning schizophrenia. The behavioural family management involved the patient and the parents in a behaviourally orientated home-based problem-solving therapy consisting of education about schizophrenia, problem solving, and communication-skills training. A more detailed description of the treatment study and protocol is provided by Falloon *et al* (1984).

Patient and family assessment

The patients' clinical symptoms were assessed monthly using the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962) by raters blind to the patient's treatment. Four factors were derived from the BPRS: schizophrenic thought, withdrawal, hostile-suspiciousness, and depression-anxiety.

The criteria used to define relapse in the present study were twofold: the treating team's unanimous decision that the patient exhibited an exacerbation of schizophrenic symptoms, and a marked elevation on blind clinician ratings of two or three florid symptoms of schizophrenia idiosyncratic to each patient (target symptom ratings, TSR). Ten patients met one or both criteria for relapse at nine months (nine in the individual group and one in the family group). Fourteen patients met one or both criteria for relapse at two years (12 in the individual group and two in the family group). A more detailed description is provided by Falloon *et al* (1985).

All patients and their parents participated in an assessment procedure after the four-six-week stabilisation phase of the study and before beginning the treatment protocol (pre-therapy) and participated in the same procedure after three months of treatment (post-therapy). Pre-therapy and post-therapy assessments included two ten-minute face-to-face interaction tasks, from which both the relative's AS and patient's CS were derived. These entailed problem-solving discussions on issues of current concern to the family: one focused on the patient, the other on a family issue. A more detailed description of the interaction task is provided by Doane *et al* (1981).

From the 20 minutes of interaction, the patient's CS was rated. The CS system (Strachan *et al*, 1989) rates the manner in which patients interact with relatives during the task. Seven types of behaviour are rated: three are considered to diminish tension (autonomous statements, self-affirmation statements, support statements), three are considered to exacerbate tension (critical statements, refusals, and self-denigrating statements), and one is considered neutral (partial autonomous statements).

The interactions in the present study were rated by two coders blind to both the treatment group and patient and family characteristics. Reliability of the coding system was calculated from independent ratings of the coders on another sample of 36 families. Kappa statistics (Cohen, 1960) for each of the CS codes were as follows:

autonomous self-statements ($k = 0.82$), partial autonomous statements ($k = 0.74$), support statements ($k = 0.83$), criticisms ($k = 0.86$), self-denigrating statements ($k = 0.68$), refusals ($k = 0.83$), and self-affirmation statements ($k = 0.73$).

Data analyses on the CS variables included both the seven CS codes and profiles based on the patterns of CS codes. The profiles were created by classifying each patient according to his/her dominant coping style. Four types of profiles were created. 'Autonomous' represents patients who made a large number of autonomous statements (benign); 'externalising' represents patients who made a large number of critical statements (negative). (The name 'externalising' was derived from the assumption that a large number of critical statements signifies a tendency to cope by finding fault outside oneself and blaming others.) 'Internalising' represents patients who made a large number of self-denigrating statements (negative). Finally, 'neutral' represents patients who had a low rate of all CS codes (neutral). Before treatment, 13 subjects were benign, eight were neutral, and 12 were negative; following treatment, nine were benign, 17 were neutral, and seven were negative.

The CS profiles were further classified as to whether they reduced or increased the conflict and tension in the family. Externalising and internalising profiles were termed 'negative' as they would be likely to escalate tension, while autonomous and neutral profiles were considered 'benign' as they would be likely to reduce conflict. Analyses on the CS profiles discussed below were conducted using the three classifications: benign, negative, and neutral. A more detailed description of the CS system and the development of the profiles is provided by Strachan *et al* (1989).

Analyses were conducted to investigate possible relationships between CS variables and demographic characteristics of the patient (age, sex, race, social status, and years of education) as well as characteristics of the patient's illness (number of past admissions, total months spent in hospital, age of onset, compliance over the course of the treatment study, and whether this was a first psychotic episode). Correlations between demographic and illness history characteristics and the seven CS raw scores before and after treatment were conducted, and few were significant, no more than expected by chance. Demographic and illness history characteristics were compared between the three CS profiles and revealed that CS profile is not a function of these other patient characteristics.

Results

Analyses of the CS variables from both assessments revealed significant changes in the quality of the patients' coping style over the course of treatment. Stuart-Maxwell χ^2 analyses were conducted on the CS profiles before and after three months of treatment to see if CS profiles had changed. The findings revealed a significant change in the CS profiles for the sample as a whole, with more subjects adopting a neutral CS profile following treatment ($\chi^2 = 6.23$, d.f. 2, $P < 0.05$) (see Fig. 1).

The same χ^2 analyses were conducted for each treatment group separately. There was a significant change only in the number of patients adopting the three CS profiles in the individual group, with more patients adopting a neutral profile ($n = 17$, $\chi^2 = 6.15$, d.f. 2, $P < 0.05$). The change in CS profile was not significant for the subjects in the family treatment group although the direction of change was similar to the individual group, with more subjects adopting a neutral profile ($n = 16$, $\chi^2 = 1.89$, d.f. 2, NS) (see Fig. 1). It is not possible, however, to attribute this difference

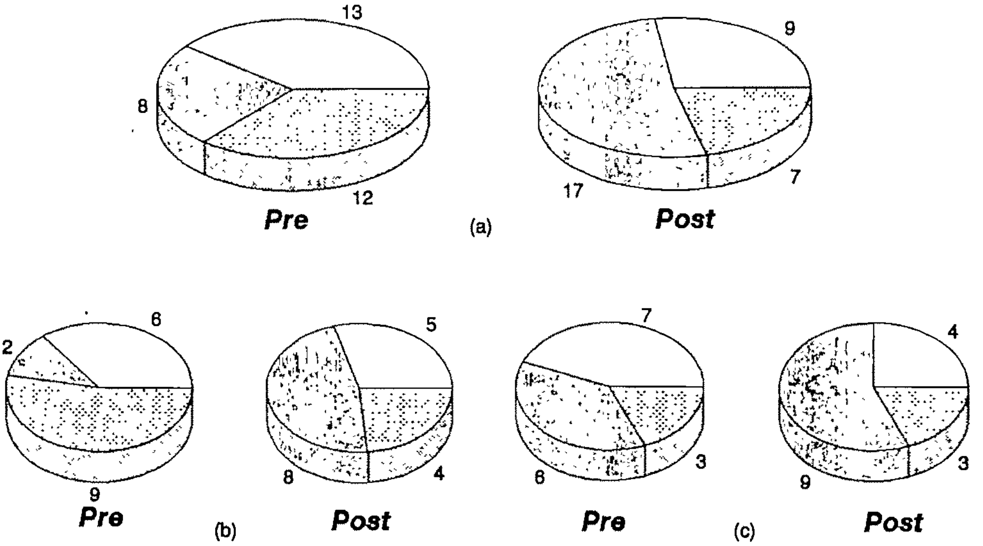

Fig. 1 Change in number of patients within each CS profile (neutral ▨ , benign □ , negative ▩) over the course of treatment: (a) total sample ($n = 33$) (Stuart-Maxwell $\chi^2 = 6.23$ ($P < 0.05$)), (b) individual therapy ($n = 17$) (Stuart-Maxwell $\chi^2 = 5.99$ ($P < 0.05$)), (c) family therapy ($n = 16$) (NS).

between the groups unequivocally to the differential effects of the treatment modalities. Despite random assignment, the groups, although not significantly different before treatment, were not identical. As evident in Fig. 1, a greater number of patients ($n=9$) had a negative profile in the individual treatment group than in the family group ($n=3$), while more patients in family treatment ($n=6$) had a neutral profile than in individual treatment ($n=2$). Thus, there was a greater possibility for change towards a neutral profile in those in the individual treatment.

In order to understand the changes in the CS of the patients more fully, analyses were conducted to assess differences in the prevalence of the various CS raw scores after three months of treatment. A series of repeated-measures analyses of variance were conducted, with treatment condition as the grouping variable and the seven CS raw scores before and after treatment as the repeated dependent factors. Analyses using the total sample revealed only one significant finding and no effects for treatment group. There was a significant decrease in the number of self-denigrating statements ($F=11.38$, d.f. 1, 31, $P<0.003$) (mean before therapy = 1.21; mean after therapy = 0.33).

Finally, we examined the relationship between CS profiles and the amount of the patient's speech during the interaction from which the CS was coded. It appeared important to examine this relationship to ensure that the change in the CS profiles over time was not solely reflective of changes in the amount of patient speech over the course of treatment. Analyses of variance were conducted, with CS profile before and after treatment and treatment group as the independent variables, and the amount of the patient's speech during the confrontation as the dependent variable. There was no significant relationship between the patient's speech before treatment and concurrent CS profile.

Finally, the role of patient speech in the change in CS profiles over time was examined. Patients were grouped, based on whether their CS profile became neutral (change), or remained benign or negative (no change), and a t-test was conducted on the difference score for the amount of patient speech over time. No significant relationships between changes in CS profile and amount of speech were found. This supported the hypothesis that the changes in CS were not simply reflective of the patients' decreased verbal production over time.

Coping style and relapse

In order to determine the relationship between a patient's CS profile and relapse, log linear analyses were conducted with the variables treatment group, CS profile before and after therapy, and relapse at nine months and two years. CS profile either before or after therapy was not predictive of relapse at nine months or two years. In contrast, as indicated in the original report by Falloon *et al* (1985), treatment group was predictive of relapse at nine months ($\chi^2=8.95$, d.f. 1, $P<0.003$) and two years ($\chi^2=15.76$, d.f. 1, $P<0.0001$), with significantly more relapses at both nine months and two years in the individual treatment group.

To examine this relationship further, a series of t-tests were conducted using relapse at nine months and two years as the independent variables and the seven CS codes as the dependent variables. No significant associations were found between the presence or absence of relapse and the prevalence of the different CS codes.

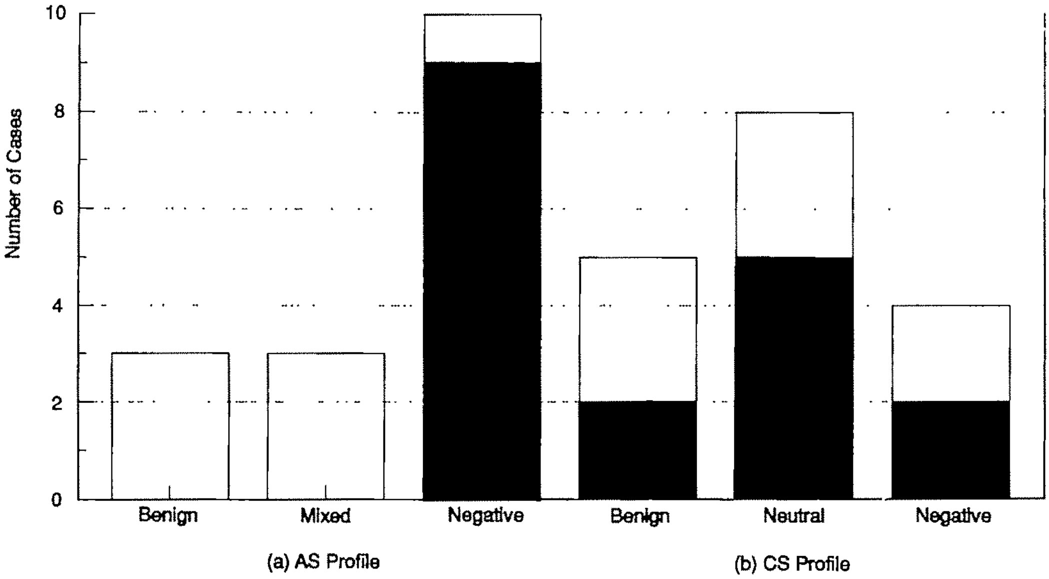

Fig. 2 The relationship of AS ($n=16$) and CS ($n=17$, an additional case added after AS analysis) profiles following treatment to relapse (■) at 9 months in the individual treatment group.

The findings did not support a consistent relationship between quality of coping style and increased rate of relapse. This is in sharp contrast to previously reported findings of a relationship between a negative AS profile following treatment and relapse rates for patients in the individual treatment group, the group in which the majority of relapses occurred (Doane *et al*, 1985). The discrepant findings between AS and CS and their relationship to relapse in the individual treatment group is depicted in Fig. 2.

Coping style and symptoms

In order to investigate any possible associations between the patients' symptoms and CS, analyses between the seven CS raw scores and the CS profiles before and after treatment, and the four BPRS factor scores (schizophrenic thought, withdrawal, hostile-suspiciousness, and depression-anxiety) were conducted. CS did not appear to be a function of current symptoms. Correlation analyses between the seven CS raw scores before and after treatment and the four BPRS factor scores at the comparable time revealed no linear relationship.

Analyses of variance revealed no significant relationship between a patient's CS profile or treatment group and concurrent BPRS factor scores, either before or after treatment. However, at the pre-therapy assessment the treatment groups differed significantly ($F=5.38$, d.f. 1, 31, $P<0.03$) on BPRS factor 4 (depression-anxiety) with the individual treatment group exhibiting a higher level of depression-anxiety. Finally, an analysis of variance was conducted comparing patients grouped with regard to their CS profile and their BPRS difference score from baseline to three months. A particular CS profile was not significantly associated with an improvement or deterioration in clinical symptoms.

Discussion

Previous analyses of the impact of family therapy as contrasted with individual therapy on relatives' AS in the study by Falloon *et al* (1984) revealed marked differences favouring family therapy (Doane *et al*, 1986). However, the present data failed to reveal comparable differences in the impact of these programmes on the patient's interactional style. Further, neither the quality of CS before or after treatment, or the nature of CS changes observed, was predictive of relapse in either treatment group. This finding differs from the data on the relatives' AS previously reported by Doane *et al* (1985, 1986). In contrast to the earlier work on the relatives' interactional style, a greater change in CS was noted in the individual treatment condition. However, it must be reiterated that the groups were not comparable at the start of treatment: the patients in the individual treatment group had more negative and less neutral profiles, and in turn a greater opportunity for change towards a more neutral stance. Thus, a differential impact of the treatment modalities cannot be unequivocally concluded from the present data. Instead, what appears important to note is that in both groups there was a systematic change towards a more neutral stance with relatives after three months of treatment. In contrast to the AS data of the relatives, neither initial nor three-month CS data in the patient were predictive of subsequent relapse.

It is difficult from these data to account for the positive therapeutic impact of family programmes on schizophrenics in terms of their impact on patient interactional behaviour. It could be concluded that changes in the patient's interactional style are not necessary for a psychoeducational family programme to achieve a positive effect on the patient's short-term course. This conclusion would agree with the findings of Leff *et al* (1989), who claimed that for those relatives who consistently attended a relatives' group without patient participation, the group condition was as effective as family programmes in reducing relapse after discharge from hospital.

However, before we accept such a radical conclusion it would be valuable to examine alternative explanations for the present data. The fact that the follow-up assessment of CS occurred after three of the nine months of treatment is noteworthy. Although this is the time during which the relatives showed marked changes in AS behaviour, it is possible that there are different rates of change for the patient over the course of a nine-month treatment programme. Three months might be adequate for relatives to begin to assimilate the skills and information being presented in the treatment and to alter their modes of interacting. In contrast, patients might require additional time to digest and incorporate the new communication and problem-solving strategies as they are attempting to recompensate from an acute episode as well as assimilate the new skills. Perhaps greater changes in CS in the family treatment group and a stronger relationship with rate of relapse would have been evident if the follow-up assessment had been repeated at six and nine months; this could have maximised the probability that the patient could alter his/her modes of communicating and problem solving.

Another explanation is that CS is not an adequate measure of the interactional style of the patient so it would not be sensitive to possible changes induced by a family therapy programme. However, the work of Strachan *et al* (1989) argues against this hypothesis and supports the validity of the CS as a measure of the patient's mode of dealing with relatives: they found that patients interacting with high-EE parents made fewer autonomous self-statements and more criticisms when compared with patients interacting with low-EE parents. It is important to note that, in the present study, neither the CS codes nor the profiles were significantly associated with BPRS scores. Thus, the CS system does not appear to be simply a measure of the patient's clinical status.

Our conclusion is that the relatives are at a higher level of functioning and can incorporate the new skills at a faster rate than the patients. In turn, this change in the relatives appears to be necessary for subsequent change in the patient's interactional style, and a more positive course. If the relatives do not change, then it is unlikely the patient will change, resulting in a higher risk of relapse. This hypothesis is supported by the work of Doane *et al* (1986) in which parents whose AS remained negative at three months tended to have schizophrenic offspring who were more likely to relapse. Thus, further research would benefit from assessing changes in patient interactional style at later points along the course of treatment, as well as the relationship of these changes to the course of the illness.

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Negative Modes of Relating, Marital Quality and Depression

JOHN BIRTCHNELL

Young married couples, with or without a depressed wife, were divided into three groups according to marital quality. Negative modes of relating were assessed by self-rating and partner-rating questionnaires. The intercorrelation of scores for different modes of relating was higher on partner-rating than on self-rating scales. There was a significant gradient of mean negative-relating scores across the three levels of marital quality. The partner-ratings of depressives and their husbands were higher on all negative-relating scales than those of non-depressed women and their husbands. The self-ratings of the depressives corresponded with these negative ratings while those of their husbands did not. The partner-rating scores differentiated between the depressives with poor marriages and those with better marriages.

The association between dependence and depression is well established (Bemporad, 1980; Birtchnell, 1984) and a number of studies have shown that depressives have high mean dependence scores (Blatt *et al*, 1982; Birtchnell & Kennard, 1983*a*, Pilowsky & Katsikitis, 1983; Hirschfeld *et al*, 1983*a*). The association between poor marital quality and depression is also well established and a number of studies have shown that depressives have poorer marriages than non-depressed controls (Weissman & Paykel, 1974; Coleman & Miller, 1975; Rutter & Quinton, 1977; Waring *et al*, 1981; Birtchnell & Kennard, 1983*b*; Waring & Patton, 1984; Merikangas *et al*, 1985; Birtchnell, 1988*a*). To complete the triangle, dependence, in at least one marital partner, is considered to be an important contributor to poor marriage (Eichenbaum & Orbach, 1983; Rubin, 1985; Birtchnell, 1986*a*), although this has not been empirically demonstrated.

Theorists have long considered dependence to be a predisposing factor for depression (Chodoff, 1972; Blatt, 1974; Nemiah, 1975; Hirschfeld *et al*, 1976; Millon, 1981). Recent studies have shown, however, that subjects with high levels of dependence do not carry an increased risk for subsequent depression (Andrews & Brown, 1988; Rossmann, 1988; Hirschfeld *et al*, 1989). This, coupled with the fact that recovered depressives have higher dependence scores than never-depressed subjects (Hirschfeld *et al*, 1983*b*, 1989) would suggest that depression induces dependence rather than results from it. It is unlikely that the picture is as clear-cut as this and the proposed association between dependence and poor marriage may represent an additional link in the causal chain.

Dependence is a complex concept (Birtchnell, 1988*b*) which can be taken apart in a variety of ways. One is within a two-dimensional framework (Birtchnell, 1987), the horizontal dimension being involvement v. separation, and the vertical one, relating from a position of strength v. relating from a position of weakness. On the horizontal dimension, dependence is concerned with seeking close involvement, and on the vertical dimension, with seeking approval and reassurance from a position of weakness. Its association with depression may be different on each dimension. On the horizontal dimension depression may be due to the breaking of close affectional ties (Bowlby, 1977), and on the vertical dimension it may be due to a fall in status (Price, 1967; Price & Sloman, 1987). This kind of differentiation has connections with other classifications of psychiatric symptoms within a two-dimensional framework (Adams, 1964; McLemore & Benjamin, 1979; Wiggins, 1982; Kiesler, 1983).

The same two-dimensional classification also has relevance to the marital relationship. Ryle (1966) proposed that poor marital adjustment may be characterised by low levels of affection (horizontal) and by dominance/submission conflicts (vertical). On the basis of this he constructed two 'marital patterns' questionnaires (Ryle, 1966; Birtchnell, 1985), subsequently modified by Scott-Heyes (1982), by which each partner makes a self-assessment and a partner-assessment of affection given and received and of relative dominance. For the present study two new questionnaires were constructed which, like Ryle's questionnaires, required each partner to make both a self-assessment and a partner-assessment, but which were intended to measure dependence and two other modes of relating called 'directiveness', the tendency to control and dictate from a position of relative strength (the opposite of the vertical component of dependence), and 'detachment', the tendency to remain distant and uninvolved (the opposite of its horizontal component). Whereas Ryle's questionnaires listed the self-assessments and partner-assessments successively on the same form, the new questionnaires used separate forms. The partner-assessment form also included a measure of dependability.

Both Ryle's questionnaires and the new questionnaires measure what might be termed 'modes of relating'. Modes of relating may be either positive or negative, the positive promoting good/constructive relationships and the negative promoting poor/destructive ones. Giving and receiving affection are positive, whereas dominating and submitting are more likely to be negative. While there clearly are positive forms of dependence, directiveness and detachment, the questionnaires were designed to measure the more negative forms. Dependability is obviously positive. Modes of relating need to be distinguished from marital quality, which includes not only how each partner feels and behaves towards the other but what actually happens between them. The study examined measures on both questionnaires in relation to (a) depression and (b) marital quality, which were assessed independently. It also compared self-assessments with partner-assessments.

In a previous study (Birtchnell, 1985) the earlier version of Ryle's Marital Patterns Test, completed only by the wife, was used to examine the marriages of women aged 40–49 years. Scores for affection given and affection received were significantly associated and were significantly lower in marriages which were assessed as poor by a semistructured interview. Poor marriages were also characterised by wife domination. A series of (mainly depressed) psychiatric patients had poor marriages with low exchange of affection but were characterised by husband domination.

Method

The index group comprised 86 couples from a housing estate in south-east London, who had formed part of an investigation of depression in 25–34-year-old married women (Birtchnell, 1988*a*). These couples had been screened by their general practitioners, using a specially designed 16-item depression screening instrument (DSI; Birtchnell *et al*, 1989). The 46 women whose scores were above a predetermined cut-off point (representing 10.5% of those screened) received the Present State Examination (PSE; Wing *et al*, 1974) and a 'caseness' level of depression at or above a CATEGO ID rating of five (Wing *et al*, 1978) was confirmed. Forty women with scores below the cut-off point on the DSI (randomly selected from the 45.3% of those screened who were within this range) were confirmed by PSE as being symptom free. Subsequently, the DSI was administered to the women's husbands. Only four husbands had scores above the cut-off point, three being married to women from the high-scoring group. These couples were also given the Ryle/Scott-Heyes Marital Patterns Questionnaire (R/S-HMPQ), as well as the new questionnaires. The quality of their marriages was assessed by semistructured interview.

A comparison group comprised 63 couples from 16 branches of Relate (formerly the Marriage Guidance Council). These couples had no assessment of depressed state, although it is likely that many would have exhibited some degree of depression, and no formal assessment of marital quality. They were however all considered by their counsellors to have serious marital difficulties. They were not given the R/S-HMPQ.

For psychometric evaluation of the new questionnaires, the two study samples were supplemented by a further 98 couples from a mixture of clinical and population sources, thus creating a total of 247 couples (494 subjects).

Both the R/S-HMPQ and the new questionnaires required the husbands and the wives to assess both themselves and their parents. Each partner was instructed to complete the questionnaires alone. The R/S-HMPQ is made up of 24 paired items (total 48 items); the first of each pair refers to the subject, the second to the partner. Thirteen items contribute to a score for affection given and 13 to a score for an affection received. These items are so broad ranging that they could be referred to as a measure of favourable disposition. Ten paired items contribute to a dominance score. Three of these items are different in the husband and wife versions. This score is a measure of relative dominance, since a point is allocated only if the subject rates him/herself as being different from his/her partner. The score is plus one if the husband is the more dominant and minus one if the wife is the more dominant. Ten is added to the total in order to eliminate minus scores. This comparative measure is unsatisfactory because it provides no indication of how dominant or submissive, in absolute terms, each partner might be. There are two unscored items.

The new questionnaires were developed to coincide with recent theoretical developments (Birtchnell, 1986*a*,*b*, 1987) and were briefly reported upon earlier (Birtchnell, 1988*c*). Copies, and scoring instructions, are available from the author on request. The self-rating questionnaire is the same for both partners. The partner-rating questionnaires differ slightly to take account of differences in emphasis and form of expression of husbands and wives. The self-rating questionnaire has 92 scored items; the partner-rating questionnaires have 83 scored items each. The items in all three questionnaires have the three possible responses of true (scoring 1 or 0 depending on the question), not sure (scoring 0.5) or untrue (scoring 1 or 0).

The semistructured interviews to assess quality of marriage were carried out in the couples' homes. The wife and the husband were interviewed by the author separately, and together. The interviews were based on the same standard schedule for each partner. Points were allocated for evidence of marital maladjustment. The individual interview covered quality of own and partner's relationship with in-laws, overall rating of partner as a person, knowledge of partner's extramarital relationships, partner's involvement with drink or drugs, partner's behaviour, deterioration in partner's attitude and behaviour, whether, as a couple, they were well suited, whether they got on well together and whether they had grown further apart.

The joint interview covered satisfaction with being able to go out separately or with the extent to which they go out as a couple, with time spent in each other's company, time spent talking together, with who talks most and the topics discussed; whether each sees the other's point of view; frequency and extent of arguments, ease with which arguments are resolved; extent to which one partner dominates or is caring towards the other; and their opinion of the effects the children have on the relationship.

In the individual interviews, the maximum possible maladjustment score was 47 for each partner (total = 94). If, for example, each in his/her respective interview considered that they had grown further apart, each was allotted points for this item. In the joint interview, the maximum score was 120, and the opinion of each partner was sought on most items. If, for example, each maintained that the other was not usually able to see his/her point of view, each again accumulated maladjustment points. The maximum possible score was 214. The couples were then divided into three study groups: the 25 with the worst marriages, the 24 with the best marriages, and the other 37. The scores of the worst couples ranged from 60 to 148. Those of the best couples were 16 or less. Such a division leads to a categorical rather than a continuous analysis but separating out an intermediate group reveals more clearly the characteristics of the indisputably poor and the indisputably good marriages.

Because of the close association between depression and poor marriage, only two of the couples with the best marriages included a depressed wife and only two of the couples with the worst marriages included a symptom-free wife (one of whom was married to a depressed husband). Since, however, only 23 of the 46 depressed women were in the worst marriage group and only 22 of the 40 symptom-free women were in the best marriage group it is possible, within the depressed and symptom-free groups, to consider the relationship between poor modes of relating and marital quality. Beyond this, it must be remembered that, since few of the husbands were depressed, such a relationship is easier to examine for them.

It has already been demonstrated (Birtchnell, 1988*a*) that a relatively high proportion of depressives have poor marriages. It is predicted that poor marriages will be associated with low exchange of affection, high domination by one partner, low dependability and high dependence, directiveness or detachment in one or both partners. It is further predicted that the depressives will have relatively high dependence scores, but their husbands will have relatively high directiveness and detachment scores, and this tendency will be particularly marked in depressives who have poor marriages.

Results

R/S-HMPQ data

As the R/S-HMPQ is well established, its psychometric properties are not considered in detail. There was, however, a highly significant correlation between subjects' scores for affection given and affection received and between ratings of affection given by one partner and affection received by the other.

For both husbands and wives, scores for affection given and affection received, and therefore mean scores for total affection exchanged, decreased significantly from the best (husbands 22.0 (s.d. 3.4), wives 22.0 (s.d. 3.9)) to the worst (13.3 (5.4), 11.5 (5.6) respectively)) marriages ($F = 21.74$, $P < 0.001$, $F = 29.12$, $P < 0.001$, respectively). The correlation of the ratings of the depressed and the non-depressed members of the worst marriages (all but one of the worst marriages included a depressed member, but only two included two depressed members) indicates that an adverse view of either self or partner was not simply a manifestation of the subject's depressed state. With regard to the relative domination scores, on both the husband and the wife ratings, there was a tendency for the wives in the worst marriages to be more dominant. The mean scores on the scales of the R/S-HMPQ for the depressed and the non-depressed women were presented in a previous publication (Birtchnell, 1988*a*). Affection given and affection received as reported by both the wives and the husbands was significantly less for the depressed couples, but there was no significant difference between the two groups in respect of relative dominance.

Birtchnell questionnaires

The following indicators of reliability for the new self-rating and partner-rating questionnaires were calculated from the larger sample of 247 couples. The self-rating questionnaire as a whole had an α reliability of 0.84. A disproportionate number of its 92 items (43) contributed to the measure of dependence. They had an α reliability of 0.82. The reliability of the 22 directiveness items was 0.74 and of the 27 detachment items was 0.78. The wife's partner-rating questionnaire (wife's rating of husband) had an α reliability of 0.76. The reliability of the 19 dependence items was 0.77, of the 29 directiveness items was 0.91, of the 15 detachment items was 0.82, and of the 20 dependability items was 0.92. The equivalent reliabilities for the husband's partner-rating questionnaire were 0.83 (total), 0.80, 0.93, 0.79 and 0.89.

For the self-rating questionnaire, there was no significant correlation between the dependence and the detachment scales ($r = 0.07$). There was low correlation between the dependence and the directiveness scales ($r = 0.13$, $P < 0.02$) and moderate correlation between the detachment and the directiveness scales ($r = 0.34$, $P < 0.001$). For the partner-rating questionnaires the correlations were generally much higher and were significant at well beyond the 0.001 level of probability. There was, as would be expected, a high negative correlation between the dependability scale and the three negative scales. For the wife's questionnaire r was -0.45 (dependence), -0.64 (directiveness) and -0.69 (detachment); the equivalent values for the husband's questionnaire were -0.38, -0.67 and -0.60. The correlations between dependence and detachment were 0.44 for the wife's questionnaire and 0.30 for the husband's; between dependence and directiveness the values were 0.49 and 0.53; and between detachment and directiveness they were 0.60 and 0.65. These differences between the self-rating and the partner-rating questionnaires are of considerable interest, particularly because the items within the two types of questionnaire were similar. They may suggest that, although individuals can be discriminating when describing their own interpersonal attitudes, when describing those of their partners they tend to answer in either a globally positive or a globally negative way.

Negative modes of relating and depression

The mean scores on the scales of the self-rating and partner-rating questionnaires are shown in Table 1. The scores on the dependability scale, although significant in the anticipated direction, were considered to be of limited usefulness (see next section). Contrary to expectation, the depressed women registered themselves significantly higher scores on all three negative modes of relating scales, and these judgements were confirmed by their husbands' rating of them. They also registered their husbands as being significantly higher on the three negative scales, whereas their husbands' ratings of themselves on these scales were only slightly higher than those of the non-depressed women's husbands, and attained a low level of significance only on the dependence scale. When the separate self-rating items of the depressed and the non-depressed women were compared, using Kendall's tau correlation as a measure of the strength of association, 53 items (listed in Appendix 1) significantly differentiated between the two groups at a level of probability of less than 0.05 and 35 did so at a level of less than 0.01. By descending order of magnitude of tau, 14 of the first 18 items were dependence items, but only five of the next 18 items were, the remainder being seven directiveness items and six detachment items.

Negative modes of relating and marital quality

Ratings on the dependability scale were high in all groups: even 9 of the 25 husbands with the worst marriages gave their wives a score which was within two of the maximum. This limited the usefulness of the measure. The dependability scores were, however, low in really poor marriages. For the worst marriages they were 14.6 (s.d. 3.7) for the husbands' rating of their wives, and 13.8 (s.d. 5.0) for the wives' rating of their husbands. For the Relate couples the equivalent scores were 11.5 (s.d. 4.4) and 10.3 (s.d 5.4), and for the best marriages they were 18.2 (s.d. 0.9) and 18.8 (s.d. 1.3). These differences are highly significant.

For both husbands and wives, on all three negative scales (i.e. excluding dependability) and, therefore, also on the summation of the three scales, there was a significant increase in mean partner-rating scores from the best to the worst marriages (Table 2); the worse the marriage the more dependent, directive or detached the partner was judged to be. The mean scores of the couples attending Relate were even higher than those of couples with the worst marriages. In contrast to the Ryle/Scott-Heyes findings (which showed only a non-significant tendency for wives in poor marriages to be more dominant) for both husbands and wives, the scale which demonstrated the most marked increase in mean scores was the directiveness scale.

There was again an increase in mean scores from the best to the worst marriages for the self-rating questionnaires, but the increase was less marked, particularly for the husbands. The range of the husbands' mean scores on the directiveness scale, which had been so discriminating with the partner-rating questionnaire, was small and non-significant. It is possible that the mean scores for the wives with the worst marriages might have been elevated simply by the women's depressed state since dependence is known to be increased in states of depression (Hirschfeld *et al*, 1983*a*,*b*). The mean dependence score was, in fact, higher for these women than for the Relate women, although not markedly so. It would, of course, be reasonable to assume that, because of their marital circumstances, many of the Relate women would also have been experiencing a degree of depression. The overall conclusion from these comparisons is that subjects in

Table 1

Mean[1] scores on the self-rating and partner-rating questionnaires for the depressed and non-depressed wives and husbands

	Husband				Wife			
	dependence	directiveness	detachment	total	dependence	directiveness	detachment	total
Self-rating questionnaire								
Depressed	18.4	11.2	10.0	39.6	24.7	11.2	9.2	45.2
(*n*=46)	(7.3)	(4.0)	(5.0)	(11.2)	(6.6)	(3.6)	(2.9)	(7.3)
Non-depressed	15.2	10.3	8.8	34.3	15.5	8.0	6.1	29.6
(*n*=40)	(6.2)	(3.6)	(3.9)	(8.9)	(5.5)	(3.2)	(3.1)	(7.8)
t	2.07*	0.90	1.35	2.33*	7.08***	4.37***	4.61***	9.53***
Partner-rating questionnaire[2]								
Depressed	8.9	9.6	4.9	23.3	5.8	7.4	4.7	17.8
(*n*=46)	(3.8)	(6.2)	(3.2)	(10.7)	(2.7)	(5.5)	(2.6)	(8.7)
Non-depressed	5.1	4.2	3.2	12.1	3.0	3.5	2.5	9.5
(*n*=40)	(3.1)	(3.6)	(2.1)	(6.7)	(2.6)	(3.9)	(1.6)	(6.7)
t	5.14***	4.56***	3.04**	5.72***	4.03***	3.62***	4.74***	4.93***

*$P<0.05$, **$P<0.01$, ***$P<0.001$.

1. Figures in parentheses are standard deviations.
2. Husband rates wife, wife rates husband.

Table 2
Mean[1] scores on the partner-rating and self-rating questionnaires by quality of marriage

	Husband				Wife			
	dependence	directiveness	detachment	total	dependence	directiveness	detachment	total
Partner-rating questionnaires[2]								
Best	4.3	3.3	2.9	10.5	3.5	2.8	2.4	8.7
($n=24$)	(3.2)	(2.7)	(2.1)	(6.3)	(2.7)	(2.8)	(1.6)	(5.6)
Intermediate	7.4	5.5	3.6	16.5	4.5	5.0	3.2	12.7
($n=37$)	(3.9)	(4.3)	(2.0)	(7.9)	(2.6)	(3.9)	(2.2)	(6.7)
Worst	9.2	12.8	5.9	27.8	6.2	9.2	5.5	20.80
($n=25$)	(3.1)	(5.7)	(3.6)	(10.4)	(2.8)	(6.4)	(2.5)	(10.0)
F	12.58***	32.44***	9.43***	37.12***	6.21***	12.58***	14.00***	16.56***
Relate	9.1	13.6	7.5	30.2	7.8	12.8	8.0	28.6
($n=63$)	(4.4)	(7.4)	(3.9)	(11.5)	(3.8)	(6.9)	(3.4)	(10.2)
Self-rating questionnaires								
Best	14.8	9.5	7.5	30.3	15.9	7.3	6.3	29.6
($n=24$)	(6.6)	(4.5)	(3.1)	(11.0)	(6.3)	(3.3)	(3.1)	(9.0)
Intermediate	15.9	11.0	9.6	36.4	20.5	9.8	7.8	38.3
($n=37$)	(6.2)	(3.5)	(4.6)	(8.7)	(7.6)	(3.3)	(3.7)	(10.3)
Worst	20.2	11.9	10.7	42.9	25.0	11.4	9.3	45.8
($n=25$)	(7.5)	(3.4)	(5.0)	(11.1)	(6.3)	(3.8)	(2.4)	(6.7)
F	4.77**	2.45	3.61*	8.12***	10.72**	14.73***	5.15***	19.66***
Relate	19.7	12.2	10.5	42.5	22.8	11.1	8.3	42.1
($n=63$)	(7.5)	(3.8)	(4.3)	(9.6)	(6.6)	(3.1)	(4.3)	(8.8)

*$P<0.05$, **$P<0.02$, ***$P<0.001$.
1. Figures in parentheses are standard deviations.
2. Husband rates wife, wife rates husband.

the worst marriages, by their own admission, tend to interact worse than subjects in the best marriages.

Extent of agreement between partner-ratings and self-ratings

In order to compare the Birtchnell questionnaires, it was necessary to remove the dependability items from the partner-rating questionnaires. When this was done, the outcome of the comparisons for the housing-estate couples and the Relate couples (using the summation of the three critical scales) was different. For the housing-estate couples, the correlation between the wife's assessment of husband and the husband's assessment of self was surprisingly low ($r=0.13$), whereas that between the husband's assessment of wife and wife's assessment of self ($r=0.47$) was highly

Table 3
Mean[1] scores on the partner-rating questionnaire

	Husband's rating of wife				Wife's rating of husband			
	dependence	directiveness	detachment	total	dependence	directiveness	detachment	total
Depressives:								
worst marriages	9.3	12.8	6.0	28.0	6.1	9.1	5.5	20.6
($n=23$)	(3.1)	(5.9)	(3.7)	(10.6)	(2.8)	(6.6)	(2.6)	(10.1)
Remaining depressives	8.4	6.3	3.9	18.7	5.4	5.7	3.9	15.0
($n=23$)	(4.3)	(4.6)	(2.0)	(8.7)	(2.7)	(3.5)	(2.4)	(5.9)
Non-depressed:								
worst/intermediate	5.5	4.7	3.2	13.4	3.8	4.5	2.8	11.1
($n=18$)	(2.7)	(4.5)	(2.0)	(7.1)	(2.5)	(4.8)	(1.8)	(7.8)
Non-depressed:								
best marriages	4.5	3.5	2.9	11.1	3.2	2.8	2.2	8.1
($n=22$)	(3.3)	(2.7)	(2.1)	(6.3)	(2.6)	(2.9)	(1.5)	(5.5)
F	9.79*	18.17**	6.24**	17.49**	5.83**	7.29**	10.22**	11.23**
Relate	9.1	13.6	7.5	30.2	7.8	12.8	8.0	28.6
($n=63$)	(4.4)	(7.4)	(3.9)	(11.5)	(3.8)	(6.9)	(3.4)	(10.2)

*$P<0.05$, **$P<0.001$.
1. Figures in parentheses are standard deviations.

Table 4
Mean[1] scores on the self-rating questionnaire

	Husband				Wife			
	dependence	directiveness	detachment	total	dependence	directiveness	detachment	total
Depressives:								
worst marriages	20.4	11.7	10.5	42.6	25.5	11.7	9.3	46.5
($n=23$)	(7.7)	(3.4)	(5.0)	(11.5)	(6.4)	(3.9)	(2.4)	(6.5)
Remaining depressives	16.4	10.6	9.5	36.5	24.0	10.7	9.1	43.9
($n=23$)	(6.5)	(4.5)	(5.1)	(10.3)	(6.9)	(3.4)	(3.3)	(7.9)
Non-depressed:								
worst/intermediate	14.9	10.8	9.8	35.5	16.8	8.5	6.4	31.7
($n=18$)	(5.5)	(3.2)	(3.9)	(8.0)	(6.1)	(2.4)	(3.5)	(7.8)
Non-depressed:								
best marriages	15.1	10.1	7.6	32.8	14.9	7.1	6.1	28.2
($n=22$)	(6.8)	(4.2)	(3.2)	(9.4)	(5.3)	(3.4)	(3.1)	(8.0)
F	3.20*	0.67	1.79	3.89**	15.32***	8.51***	6.77***	30.86***
Relate	19.7	12.2	10.5	42.5	22.8	11.1	8.3	42.1
($n=63$)	(7.5)	(3.8)	(4.3)	(9.6)	(6.6)	(3.1)	(4.3)	(8.8)

*$P<0.05$, **$P<0.02$, ***$P<0.001$.

[1] Figures in parentheses are standard deviations.

significant. Either the wives were poor judges of their husbands or the husbands were denying certain features in themselves which were apparent to their wives. For the Relate couples, the correlations were moderately high for both ($r=0.37$ and 0.33 respectively) and again, highly significant. In the mixed sample of 247 couples (which included the two study samples) it was possible to consider the correlations between partner-ratings and self-ratings for the separate scales. For dependence, r was 0.41 and 0.42, for directiveness it was 0.30 and 0.36, and for detachment, it was 0.26 and 0.41 for wives and husbands respectively. There were no significant correlations across scales.

Negative modes of relating by quality of marriage within the depressed and the non-depressed groups

Since the measures of negative modes of relating are significantly related both to depression and to poor marital quality, it seems likely that there would be a gradient of scores ranging from the depressives with the worst marriages to the non-depressed women with the best marriages. Tables 3 and 4 show this to be the case, particularly for the husbands' ratings of their wives. The gradients were not the same, however, for all scales. The wives' dependence, whether measured by self-ratings or by their husbands' ratings, was markedly higher for depressives, irrespective of marriage quality. The depressives' dependence rating was higher even than that of the Relate women. Dependence is, therefore, more closely linked with depression than with marital quality. Rating the marital partner as directive (by husband or wife) was markedly associated with poor marital quality, and this was particularly apparent within the depressive group. The Relate couples had higher partner-rating scores for directiveness than even the depressives with poor marriages.

Discussion

This study was prompted by two sets of observations: the first is that the incidence of neurotic depression in young, married women is disturbingly high (Grad de Alarçon *et al*, 1975; Brown & Harris, 1978; Bebbington *et al*, 1981; Ensel, 1982); the second is that there is a significant association between depression and poor marital quality (Coleman & Miller, 1975; Rutter & Quinton, 1977; Waring *et al*, 1981; Waring & Patton, 1984; Merikangas *et al*, 1985). In two earlier reports (Birtchnell, 1988*a*; Birtchnell *et al*, 1989) both these observations were confirmed in the present population samples. Poor marital quality may lead to depression and depression may lead to poor marital quality, and it is probable that, when both are present, they reinforce each other. The association between depression and poor marital quality may be further explained by the fact that they share a common link with a third factor, namely negative modes of relating. Dependence, the most well defined of these, has been shown to be significantly related to depression and has been implicated in explanations of poor marital quality. Its link with depression has been confirmed in the present study, but the study has also demonstrated that other negative modes of relating may be linked with depression. The need for further work in this area is indicated.

Because of the close association between poor marital quality and depression, it is not easy to determine which negative modes of relating might have a direct link with poor marital quality. This could be done only with couples with neither partner depressed but poor marital quality. Because of the importance of marriage to the well-being of many young women, particularly in a working-class culture, such couples may not be common. The wife would need to have some satisfying involvement either in her work or in a relationship outside her marriage. Only one couple in the worst marriage group did not include a depressed member, and the wife of this couple had a previous history of depression. Had the study included a group of women whose depression scores were within the intermediate range, there might have been more in this category. Only the self-ratings of the husbands in the poor marriage group may be accepted as reliable indicators of poor marital quality. Their ratings of their depressed wives may be correct assessments of those modes of relating which are linked with their wives' depression and their wives' ratings of them may be either projection (in the psychoanalytic sense) or simply the way they view their husbands. The range in the mean self-rating scores of the husbands from the best to the worst marriages was significant and in the expected direction, but was far less impressive than that of their wives. This would suggest that most of the variation in the wives' scores was due to the vast majority of the women in the worst marriages being depressed. However, the self-ratings of the husbands from the worst marriages were strikingly similar to those of the husbands of the Relate couples. As well as providing confirmation of the reliability of the self-rating questionnaires, this would indicate that husbands' negative modes of relating are, to some degree, associated with poor-quality marriage. This conclusion is further supported by the fact that, within the depressed women's group, the self-rating scores of the husbands from the worst marriages remain higher, particularly on dependence.

The self-ratings of the depressed women, on all three negative measures, were markedly different from those of the non-depressed women, and the items which discriminated most significantly between the depressed and the non-depressed women came from all three negative measures. Also, the partner-ratings of the husbands of the depressed women were markedly different from those of the husbands of the non-depressed women, again on all three negative measures. These observations together provide strong evidence that depressed women relate in more than one negative way, though previous work would tend to suggest that such negative relating is less a predisposing factor than a concomitant of the depression itself. In an earlier study (Birtchnell, 1988*a*) it was reported that 44% of the women had been depressed for two years or more. For these women at least, the negative mode of relating had become well established and could well be playing a part in the maintenance of the condition.

A notable feature of the study was the low correlation between the self-ratings and the partner-ratings. This could conceivably be construed as an indication of poor validity. Reporting upon their measurement of irritability within the marital relationship, Rutter & Brown (1966) wrote "unless the account given by the husband agrees fairly well with that given by the wife there can be little confidence in the measure". In the present instance this would not be a reasonable conclusion, since the questionnaires are measuring how each partner *perceives* him/herself and the other. A person's perception of another may be quite different from the other's perception of him/herself, but this does not invalidate the measures. Although the depressed women's assessments of themselves corresponded closely with their husbands' assessments of them, their assessments of their husbands corresponded very poorly with their husbands' assessments of themselves. If the measures were simply invalid, the disagreements would have been similar for both types of comparison. Since they were not, there has to be an explanation for the difference. Either the depressed wives were wrong about their husbands or their husbands were wrong about themselves. Again, the wives may have been projecting their own characteristics on to their husbands, or their depression may cause them to misperceive their husbands. It is possible, however, that the wives' depression was being both generated and maintained by their husbands denying the deficiencies which their wives were correctly ascribing to them.

In the self-rating questionnaires, the three negative scales were reasonably independent of each other; in the partner-rating questionnaires, they showed a considerable degree of intercorrelation. Since this applied so much more to one kind of questionnaire than to the other it is unlikely to be due either to a conceptual overlap or to the possibility that the three modes of relating tend to occur together. The explanation is probably that individuals will differentiate between their own modes of relating, but are inclined to make more global judgements about their partners'. When they feel well disposed towards them they tick mainly positive statements, when they do not, they tick mainly negative ones, in a fairly indiscriminate way. This unfortunate tendency would interfere greatly with the use of questionnaires for the identification, in specific terms, of one partner's assessment of the other's modes of relating, and would limit them to simply recording a generally positive or negative disposition of one partner towards the other.

It would be wrong to conclude that the division of the partner-rating questionnaires into separate scales had been a worthless exercise. The mean scores on the directiveness scale were of particular interest.

The depressed women and their husbands rated their partners more highly on this scale than did the non-depressed women and their husbands; within the group in which the wives were depressed, the couples with the worst marriages rated each other higher still. The partner ratings on directiveness of the Relate couples were higher even than this. Price & Sloman (1987) have developed an evolutionary model of depression, in which they propose that depressed mood accompanies yielding to a dominant other in a situation of social competition. Price (1988) has applied this model to the marital relationship and describes the marital "slanging match" as a competition in which each contestant continues verbally to assert his/her superiority over the other. Theories of depression in terms of dominance/submission conflicts have also been proposed by Feldman (1976), Coyne (1976), and Kiesler (1986). It was predicted that the present study would show depressed women to be excessively dependent and their husbands excessively directive, on the expectation that their dependence would represent a kind of yielding to their husbands' directiveness. The results suggest that they perceived themselves and were perceived by their husbands both as yielding and as fighting back. It was perhaps surprising that the same finding did not emerge from the domination scale of the R/S-HMPQ. This may be because it is a comparative measure and only registers if one partner is more dominant than the other. If, as the results suggest, both partners are inclined to be dominant, the responses would cancel each other out.

The study convincingly shows that dependence is not the only negative mode of relating to be associated with depression and poor-quality marriage. Further work is needed in the refinement of the present measures and in the development of new ones. More needs to be done in the classification of modes of relating and in establishing more clearly their relationship to depression and also to other psychiatric conditions. Their relationship to marital quality needs to be explored in non-depressed couples with poor marriages. Because of the tendency for married partners to respond in either a generally positive or a generally negative way in response to statements about each other, the further development of partner-rating questionnaires may be limited. Selecting out items which correlate across scales will hopefully reduce this problem. Greater reliance may, however, need to be placed upon self-rating questionnaires.

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Appendix

The self-rating items which significantly ($P<0.05$) discriminated between the depressed and the non-depressed women (Kendall's tau in parentheses) (p = dependence, r = directiveness, t = detachment).

p	I am well pleased with myself (−0.63)
p	I can never convince myself that people really love me (0.61)
p	It takes a lot to unsettle me (−0.61)
p	I have a dread of being rejected (0.58)
p	I am not very sure where I am going in life (0.57)
p	Even the slightest criticism can affect me for hours (0.56)
p	I can never be sure that people approve of me (0.55)
p	I don't feel I have very much to offer in life (0.54)
p	I am very much affected by other people's moods (0.51)
p	I am always afraid that someone I am fond of will lose interest in me (0.51)
p	I'm not very good at solving my own problems (0.48)
t	When people get too close to me it makes me uneasy (0.46)
r	I often make hurtful remarks which I later regret (0.45)
r	It disturbs me when people will not do what I expect of them (0.44)
p	When another person is depressed it tends to make me depressed (0.41)
p	When things go wrong I am all too ready to assume it's my fault (0.40)
r	I am sometimes inclined to put someone down with an unkind remark (0.37)
p	I have a tendency to admire or even idolise other people (0.36)
t	I prefer things to people because they don't let you down (0.34)
r	I worry that the person I feel close to doesn't do things right (0.32)
r	I feel I need to keep a close eye on the person I am close to (0.32)
p	I am very bad at standing up for myself (0.31)
r	I have noticed I can sometimes be very critical of someone I like (0.31)
t	I prefer to keep my feelings to myself (0.30)
p	I have no very clear-cut aims in life (0.30)
r	I find I am inclined to form a relationship with someone who is weaker than me (0.29)
r	I am inclined to be very jealous and possessive (0.28)
t	I find it necessary to get away from people sometimes (0.28)
t	I am inclined to be intolerant of other people's faults (0.28)
r	It worries me if the person I am close to has too much freedom (0.28)

p I have a tendency to look up to others (0.28)
t I would rather people didn't bother me with their problems (0.27)
t I do not like to get too involved with people (0.27)
r I have sometimes felt that if I don't take control in a relationship things could go wrong (0.27)
p I'm not inclined to ask other people to help me (−0.26)
t I do not like being left on my own (0.26)
p I pride myself on having a mind of my own (−0.26)
p I am not much affected by what others say about me (−0.25)
r Other people tend to look to me for guidance (−0.24)
t When I am upset I try not to show it (0.23)
p I don't like to push myself forward (0.21)
p I find it easy to be affectionate to the person I am close to (0.20)
t I find my own ideas more interesting than other people's (0.20)
t I usually find it easiest to abide by the rules (−0.19)
t I believe in staying cool and unruffled at all times (−0.19)
t I don't concern myself too much with other people's worries (0.19)
r I have no difficulty telling another person what to do (0.19)
r I find it easy to be caring towards another person (0.19)
r I often praise and encourage the person I feel close to (0.19)
p I prefer it when others make decisions for me (0.18)
r I mostly have a good idea what the person I feel close to needs to do (−0.18)
r I feel more comfortable in a relationship when I'm the one who makes the decisions (0.17)
p I am inclined to follow or imitate other people (0.17)

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Plasma Levels of Fluphenazine in Patients Receiving Fluphenazine Decanoate

Relationship to Clinical Response

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The levels of fluphenazine and fluphenazine sulphoxide in schizophrenic patients who were randomly assigned to receive either 5 mg or 25 mg of fluphenazine decanoate every two weeks were monitored. Patients treated with 25 mg of fluphenazine decanoate required three months to reach a steady-state plasma level, indicating that those patients who are being converted from oral to depot fluphenazine should continue to receive oral supplementation during the first three months of treatment with fluphenazine decanoate. Plasma levels of fluphenazine sulphoxide were lower than levels of fluphenazine. At six and nine months following randomisation, there was a statistically significant relationship between lower fluphenazine plasma levels and an increased risk of psychotic exacerbations. A relatively weak relationship was found between fluphenazine plasma levels and akinesia, but non-significant relationships between fluphenazine levels and other neurological side-effects including akathisia, retardation, and tardive dyskinesia. Monitoring the plasma levels may be helpful to clinicians who are attempting to treat stabilised patients with the lowest effective dose of fluphenazine decanoate.

Decision-making about drug dosage during the maintenance phase of therapy for schizophrenia is problematic, because the patient is usually clinically stable. As a result, drug dose cannot be titrated against clinical response. If the monitoring of neuroleptic plasma levels during this phase of treatment were useful, it would provide an objective method for assessing a patient's pharmacotherapy. In addition, measurement of plasma levels could provide guidance to clinicians who are trying to treat patients with the lowest effective neuroleptic dose. Recent studies (Kane *et al*, 1983; Marder *et al*, 1987; Hogarty *et al*, 1988) have suggested that a proportion of chronic schizophrenic patients can be treated with doses of neuroleptic substantially lower than those usually prescribed. Dosage reduction strategies might be carried out more safely if plasma level measurement could provide the treating physician with an indication that the patients may be receiving an inadequate dose.

Unfortunately, there have been very few studies that include measurement of plasma levels in maintenance therapy. Brown *et al* (1982) studied patients treated with one of several neuroleptics, using a radioreceptor method. They found that patients who eventually relapsed had lower anti-dopaminergic activity in serum than those who remained stable. Wistedt *et al* (1982) studied levels of fluphenazine (FLU) and a metabolite, 7-hydroxyfluphenazine, in patients who received fluphenazine decanoate (FD) (mean dose, 21.4 mg every two weeks). Patients who relapsed had lower plasma levels (mean 0.92 ng/ml) than those who did not relapse (mean 1.36 ng/ml). We (Marder *et al*, 1986) previously reported that patients who had psychotic exacerbations of their illness tended to have lower FLU plasma levels (mean 0.6 ng/ml) than those who remained stable (mean, 1.0 ng/ml). However, this difference was not statistically significant. The data in this report is from the same clinical study, but uses a larger sample and a longer observation period.

The present study monitored the plasma concentrations of FLU and an inactive metabolite, fluphenazine sulphoxide (FLUSO), in patients who participated in a previously described comparison of a low and conventional dose of FD (Marder *et al*, 1987). We addressed the following issues: (a) How long does it take patients to reach a stable steady-state when they are medicated with FD? (b) How extensively is FLU metabolised to FLUSO in patients treated with depot fluphenazine? (c) What is the relationship between the plasma concentrations of FLU and FLUSO and clinical response? (d) What is the relationship between these plasma concentrations and neurological side-effects?

Method

The subjects were 53 men referred to a specialised out-patient research clinic at the Brentwood Division of the West Los Angeles V. A. Medical Center. The details of the selection process and the study methodology are described elsewhere (Marder *et al*, 1987). All subjects fulfilled DSM-III criteria (American Psychiatric Association, 1980) for schizophrenic disorder. Diagnosis was confirmed with the Present State Examination (PSE; Wing *et al*, 1974). After giving written informed consent, subjects were stabilised for two or more months with fluphenazine decanoate (FD). Our criteria for stabilisation were as follows: (a) stability on the psychosis scores (including cluster scores for thought disturbance and paranoia) of the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962) over at least two months, with no single item increasing by more than one in any two consecutive ratings; (b) living in a stable community setting for two months; and (c) no significant change in the dose of FD during the two months before baseline. Individuals who could not be stabilised on 25 mg or less every 14 days were dropped from the study. Other exclusion criteria included organic brain disease, mental retardation, alcoholism, or other serious substance abuse. Patients were screened at baseline for drugs of abuse with urine tests and again whenever abuse was suspected. Schizophrenic patients with affective symptoms that required treatment with antidepressants, lithium, or benzodiazepines were excluded.

Following stabilisation, all neuroleptics were stopped for four weeks. This actually entailed missing one injection of FD. (Since patients who have been chronically treated with FD may have substantial plasma levels of FD for months following drug withdrawal (Wistedt *et al*, 1982; Gitlin *et al*, 1988), this brief period did not constitute a drug washout.) At this point, all subjects received a test dose of 5 mg of fluphenazine decanoate. Two weeks after the test dose, patients were randomised to a double-blind trial of 5 mg or 25 mg of FD administered every 14 days. The 25 mg doses were administered as a solution of FD (25 mg/ml) in sesame oil. In order to facilitate administration of 5 mg doses, FD was formulated as a solution of 5 mg/ml in miglyoil (custom formulation, contributed by E. R. Squibb & Co.). Blood samples for measurement of plasma levels were drawn at two, three, six, nine, 12, 15, 18, and 24 months following randomisation. Blood samples were drawn two weeks following the previous injection and just before the next injection was administered. Whole blood samples were collected in all-glass systems (Midha *et al*, 1981). Antiparkinson drugs, commonly 2–4 mg of benztropine mesylate twice daily, were administered for all patients who had a history of extrapyramidal side-effects (EPS) on neuroleptics. The dose was not changed during the course of the study, unless new EPS emerged or side-effects of the antiparkinson drug were noted. This resulted in nearly all of the patients from both dosage groups receiving benztropine.

Patients were maintained on their assigned dose for as long as they were stable. When patients demonstrated a worsening of three or more on BPRS cluster scores for thought disturbance or paranoia they were considered to have had a psychotic exacerbation. Most exacerbations were rather mild and easily managed by an increase in the patient's FD dose. Fewer than one-third of the relapses required readmission to hospital. Although 66 patients were entered into the original clinical study (Marder *et al*, 1987), 13 refused to participate in plasma-level monitoring and are therefore not included in this study. Plasma levels are included only for patients who remained stabilised on their original assigned dose at each time-point. Thus, there is a diminishing sample size that is related to patients being dropped from the analysis whenever they either exacerbated or dropped out of this study. Furthermore, plasma samples were occasionally missed on patients when they did not appear at an evaluation on schedule, or, on some occasions, samples were mishandled. Thus, at four weeks there were 49 patients in the sample, at 26 weeks, 33 patients, and at 38 weeks, 35 patients. Of the original 66 patients entered in the clinical study, 11 had had exacerbations and seven dropped out by 26 weeks. By 38 weeks, 13 had demonstrated exacerbations and nine had dropped out. Table 1 describes the demographic characteristics of patients who were evaluated at 12, 26 or 38 weeks.

Clinical outcome was assessed at the same time that plasma samples were drawn. Rating instruments included the BPRS, the Hopkins Symptom Checklist (SCL-90R; Parloff *et al*, 1954), the Involuntary Movement and Extrapyramidal Rating Scale (IMEPS), and the Subjective Extrapyramidal Rating Scale (SERS) (Marder *et al*, 1987). Side-effects were measured using the IMEPS and the SERS. To reduce the number of items in these two instruments, a principal components analysis was utilised. This yielded four main factors, akinesia, retardation, akathisia and dyskinesia.

Plasma levels of FLU were measured using a radioimmunoassay (RIA) (Midha *et al*, 1980) which was validated for specificity using gas chromatography mass spectroscopy (GCMS; Dudley *et al*, 1983). The sensitivity of the FLU method was 0.1 ng/ml and the coefficient of variation was 3%. The antisera used for the RIA did not cross-react with benztropine or other commonly used antiparkinson drugs. Levels of FLUSO were also measured by a RIA (Midha *et al*, 1987) that did not cross-react with parent fluphenazine or any of the important metabolites of fluphenazine or with antiparkinson drugs. The sensitivity of this method was 0.1 ng/ml and the coefficient of variation was <8.1%.

Table 1
Sample description for patients with plasma levels monitored at 12, 26, and 38 weeks

	5 mg group (*n*=20)		25 mg group (*n*=19)	
Mean (s.d.) age: years	37.8	(8.4)	40.3	(10.9)
Mean (s.d.) education: years	13.4	(1.7)	12.5	(2.4)
Mean (s.d.) illness duration: months	148.9	(104.8)	185.1	(102.9)
Race: no. (%)				
caucasian	5	(25.0)	9	(47.4)
black	14	(70.0)	8	(42.0)
hispanic	0	(0.0)	2	(10.5)
other	1	(5.0)	0	(0.0)
Marital status: no. (%)				
single	10	(50.0)	10	(52.6)
married	5	(25.0)	2	(10.5)
divorced	4	(20.0)	6	(31.6)
separated	1	(5.0)	1	(5.3)

Results

FLU and FLUSO levels over the two years of the study are described in Fig. 1 and Table 2 for both dosage groups. In order to calculate the time to a steady-state, we fit a segmented non-linear model to the data using an iterative curve-fitting procedure. The function we evaluated was a quadratic function in the early stage (before steady-state) that is joined to a horizontal line (plateau). The point where these two segments met represented the time at which steady-state was reached. For patients receiving 25 mg, the point at which the two segments met for plasma FLU was 11.4 weeks and the plateau was at 1.2 ng/ml. A somewhat shorter time was computed for FLUSO. On the other hand, patients treated with 5 mg FD every two weeks appeared to be at steady-state for both FLU and FLUSO at the time of randomisation, and therefore this model was not appropriate. Regression analyses of mean plasma levels of parent drug and metabolite v. time beginning at 12 weeks revealed that the slopes did not differ significantly from zero in either dosage group (Table 3). This also indicates that all analytes were at steady-state after three months of treatment. Over the 92 weeks from week 12 to 104, the coefficients of variation about the mean steady-state levels were less than 17%, with the exception of the sulphoxide metabolite in the low-dose group where the coefficient of variation was 30% (Table 3). Wider variation in the latter group probably arose because plasma levels tended to be close to the quantitation limit of the assay (0.1 ng/ml).

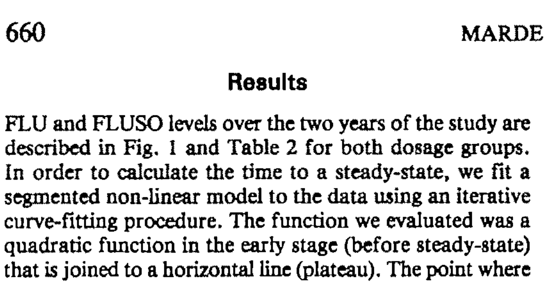

Fig. 1 Mean fluphenazine (–) and fluphenazine sulphoxide (---) levels for patients who remained on their original fixed dose of 5 (■) or 25 mg (●) of fluphenazine decanoate at each time point (means, standard deviations, and sample size for each value are included in Table 2).

Table 2 lists the means and standard deviations of plasma levels of FLU and FLUSO for patients in the two dosage groups. FLU levels were significantly higher than FLUSO levels for the two groups combined ($P = 0.0005$). When we compared the two levels in each dosage group, the difference was only statistically significant for the 25 mg group ($P = 0.0001$), but the difference between dosage groups was not significant.

The relationship between plasma levels and clinical response was studied in patients who were stabilised for three, six, or nine months on their assigned dose. We did not use plasma level values obtained before three months because they may have included patients who were not at steady-state. We were concerned that if we included individuals who had plasma levels that were still increasing or decreasing, the plasma-level measurement at the indicated time-point might not reflect the amount of neuroleptic protection the patient was receiving in the weeks before and after the blood drawing. The outcome measure we used was the occurrence of psychotic exacerbations during the year following the index plasma level.

In order to normalise the distribution of plasma concentrations, the values were log transformed. We investigated the relationship between these transformed plasma levels at three, six, and nine months and subsequent psychotic exacerbations with logistic regression. (The sample size was too small at later time points for meaningful analysis). The relationship was non-significant at three

Table 2
Mean fluphenazine and fluphenazine sulphoxide plasma levels over two years in those on dosages of 5 mg and 25 mg of fluphenazine decanoate

	Fluphenazine plasma level						Fluphenazine sulphoxide					
	5 mg group			25 mg group			5 mg group			25 mg group		
Week	$\bar{x}$	(s.d.)	*n*	$\bar{x}$	(s.d.)	*n*	$\bar{x}$	(s.d.)	*n*	$\bar{x}$	(s.d.)	*n*
Base line	0.70	(0.63)	19	0.82	(0.81)	28	0.39	(0.40)	25	0.51	(0.40)	28
2	0.69	(0.67)	21	0.85	(0.79)	26	0.57	(0.87)	22	0.51	(0.28)	23
4	0.77	(0.99)	21	1.15	(0.81)	28	0.41	(0.29)	21	0.67*	(0.50)	27
8	0.70	(0.59)	20	1.24*	(0.86)	22	0.44	(0.30)	24	0.63	(0.42)	21
12	0.67	(0.59)	20	1.47***	(0.72)	19	0.29	(0.17)	19	0.83**	(0.82)	21
26	0.73	(0.63)	16	1.48*	(1.08)	17	0.27	(0.26)	20	0.69***	(0.30)	18
38	0.61	(0.62)	16	1.67**	(1.28)	19	0.25	(0.16)	17	0.85***	(0.33)	15
52	0.44	(0.47)	13	1.27**	(0.78)	15	0.40	(0.58)	11	0.65	(0.33)	13
64	0.57	(0.51)	10	1.30*	(0.92)	16	0.31	(0.19)	10	0.80***	(0.37)	13
78	0.63	(0.57)	6	1.89**	(1.31)	13	0.42	(0.22)	5	0.74*	(0.22)	9
90	0.74	(0.79)	7	1.20	(0.59)	11	0.16	(0.12)	6	0.77***	(0.23)	9
104	0.72	(0.58)	3	1.66	(0.77)	12	0.17	(0.18)	7	0.88**	(0.52)	10

*$P<0.05$; **$P<0.01$; ***$P<0.001$ (*t*-tests for differences between 5 mg and 25 mg).

Table 3
Analysis of steady-state plasma levels from 12–104 weeks

Analyte	Dose FD: mg/2 weeks	Mean plasma concentration: ng/ml	Coefficient of variation (%)	Correlation coefficient (r)	Slope	Significance of slope (t-test)^1
Fluphenazine	25	1.50	15.78	0.07	0.0005	0.17
Sulphoxide	25	0.78	10.40	0.32	0.0008	0.83
Fluphenazine	5	0.65	16.07	0.25	0.0008	0.44
Sulphoxide	5	0.29	30.07	−0.24	0.0006	0.61

1. $n-2=6$ degrees of freedom. None of the t-tests was significant.

months ($\chi^2=0.21$, d.f. = 1, $P=0.65$), but significant at six months ($\chi^2=4.38$, d.f. = 1, $P=0.04$) and nine months ($\chi^2=6.62$, d.f. = 1, $P=0.003$) (see Fig. 2a,b). The same relationship was apparent when the mean plasma levels were compared for patients who exacerbated and those who did not (for six months, the mean FLU plasma level for patients who did exacerbate was 0.62 (s.d. 0.47) and for patients who did not exacerbate it was 1.33 (s.d 1.04), $P=0.01$; for nine months, 0.51 (s.d. 0.36) for patients who did exacerbate and 1.59 (s.d. 1.27) for patients who did not, $P=0.001$). The relationship is displayed at nine months in Fig. 3.

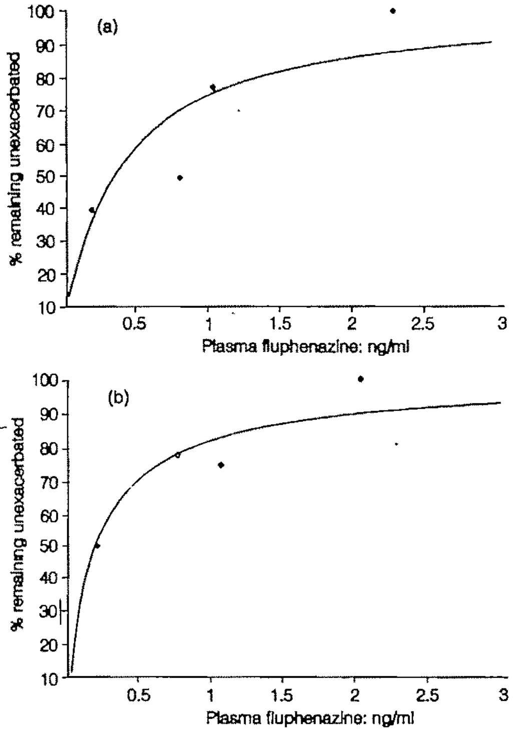

Fig. 2 Relationship between risk of psychotic exacerbations during the following year and plasma fluphenazine levels at (a) 6 months ($n=33$) and (b) 9 months ($n=35$), showing logistic regression functions (——) computed from the actual date, and the actual data points (◇) computed by ordering the plasma specimens from lowest to highest plasma level. For each quartile of the sample, the percentage remaining unexacerbated during the following year was computed and the diamond (◇) placed at the midpoint of the plasma range for each quartile. (For 6 months $\chi^2=4.38$, $P=0.04$; for 9 months, $\chi^2=8.98$, $P=0.003$.)

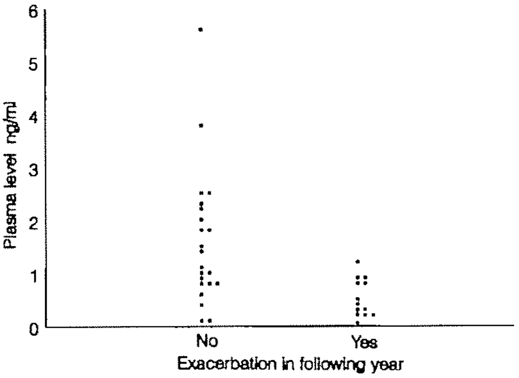

Fig. 3 Plasma fluphenazine levels drawn at nine months in patients who exacerbated (mean level = 0.51 ng/ml (s.d. 0.36) and those who did not (mean level 1.59 ng/ml (s.d. 1.27) (t-test, $P=0.001$).

The relationship between plasma level and the rate of psychotic exacerbations over the subsequent 12 months was also studied by survival analysis using the log transformed FLU levels as a covariate (Cox models) (Table 4). This method of data analysis differs from logistic regression in that it takes the length of time between the index evaluation (at three, six, and nine months) and the week in which the patient exacerbates into account. Using this method, we found a relationship between the FLU plasma level and the risk of exacerbations at six months that was nearly statistically significant ($\chi^2=3.77$, d.f. = 1, $P=0.052$) and a relationship at nine months that was significant

Table 4
Fluphenazine plasma levels as predictors of psychotic exacerbation during the following year

Evaluation: week	Survival analysis (Cox models) χ^2	P	Logistic regression χ^2	P
12	0.87	0.35	0.21	0.65
26	3.77	0.052	4.38	0.04
38	12.21	0.0005	8.98	0.003

Table 5
Relationship of fluphenazine plasma concentrations[1] and side-effects[2]

Week	(*n*)	Akinesia *R*	Akinesia *P*	Retardation *R*	Retardation *P*	Dyskinesia *R*	Dyskinesia *P*	Akathisia *R*	Akathisia *P*
2	(45)[3]	0.36	0.01	−0.11	0.48	−0.24	0.11	−0.25	0.09
4	(49)	0.29	0.052	−0.26	0.08	−0.06	0.71	−0.20	0.17
8	(42)	0.26	0.11	0.10	0.55	−0.06	0.74	0.24	0.14
12	(39)	0.15	0.37	0.07	0.67	−0.28	0.09	0.21	0.19
26	(33)	0.50	0.003	−0.09	0.60	−0.01	0.97	0.31	0.08
38	(36)	0.01	0.95	−0.24	0.18	−0.09	0.61	0.07	0.71
62	(28)	0.31	0.11	0.10	0.62	0.16	0.43	0.14	0.49

1. Fluphenazine plasma levels were evaluated as log-transformed plasma concentrations in order to normalise the distribution.
2. Side-effect values were the mean values for side-effect cluster scores derived from a principle component analysis of objective and subjective extrapyramidal scores (see Marder *et al*, 1987).
3. Sample sizes differ with those of Table 2 when patients had a plasma level specimen drawn but missed a side-effect evaluation.

($\chi^2 = 11.25$, d.f. = 1, $P = 0.0008$) (Table 4). At three months, the relationship was non-significant ($\chi^2 = 0.87$, d.f. = 1, $P = 0.65$). Using the same method (survival analysis with covariates), we did not find a statistically significant relationship between FLUSO levels and clinical response at any of the three time-points.

The relationships between neurological side-effects and plasma concentrations were evaluated using cluster scores of four side-effects (akinesia, akathisia, retardation, and dyskinesia), derived from a principal components analysis we previously reported. For this analysis we studied the correlations between the side-effects cluster and log transformed FLU concentrations. As noted in Table 5, there were statistically significant correlations between FLU levels and akinesia at two, four and 26 weeks, but not at the other evaluation times. Dyskinesia, retardation, and akathisia were not significantly correlated with plasma concentrations at any of the time points.

Discussion

We found that patients who are treated with 25 mg of fluphenazine decanoate require three months to reach a steady-state plasma level. Patients who were randomly assigned to 5 mg of FD appeared to be at steady-state when the study began. Our findings also indicate that patients treated with FD have lower plasma levels of FLUSO than FLU. At six and nine months following randomisation, there was a statistically significant relationship between fluphenazine plasma levels and the protection from psychotic exacerbations. We found a relatively weak relationship between FLU plasma levels and akinesia, but non-significant relationships between FLU levels and other neurological side-effects including akathisia, retardation, and tardive dyskinesia.

Our current data are consistent with our previous report indicating that patients treated with 25 mg of FD require approximately three months to reach a stable steady-state (Marder *et al*, 1986). Using the data from this study, we calculated an effective half-life of 2.5 weeks which would bring the plasma levels to steady-state in approximately 12 weeks (Hubbard *et al*, 1989, unpublished report). This is in close agreement with the 11.4 weeks we found by curve-fitting. Casual inspection of Fig. 1 might suggest that plasma concentrations of FLU continue to rise for 36 weeks after the assignment to dosage group. More objective scrutiny, as noted above, reveals that after 12 weeks, fluctuations in plasma levels probably represent random variations about a steady-state of about 1.2–1.4 ng/ml. A certain amount of random variation about a mean steady-state is inevitable for at least two reasons. First, there are a variety of clinical factors which can contribute to variance. For example, the pharmacokinetics of the drug may be affected over time by changes in diet, smoking habits, alcohol consumption, or abuse of street drugs. Second, there are random day-to-day variations in the drug assay that are defined by the accuracy and precision of the method, and by routine analysis of quality control samples.

The amount of time we calculated as necessary to reach a steady-state for the 25 mg dose (about 12 weeks) is similar to the 10 weeks reported by Ereshefsky *et al* (1984) in a study that monitored patients receiving weekly injections of FD. A similar time interval has also been reported for haloperidol decanoate (Reyntjens *et al*, 1982).

The length of time that it takes FD (or haloperidol decanoate) to reach a steady-state may be clinically important. If patients are abruptly changed from an oral to a depot formulation of a neuroleptic, there may be a significant period of time – perhaps 1–3 months – during which the patient may be under-medicated and therefore, more vulnerable to relapse. This possibility was confirmed by Yadalam & Simpson (1988), who reported how the FLU levels of two patients substantially decreased immediately after their change from oral to depot fluphenazine. If patients are started on higher doses of FD, the medication may appear to be well tolerated immediately following the conversion, but become excessive – or even toxic – as the patient's plasma level rises during the next several weeks. Three possible solutions to this dilemma are: (a) supplement the patient's dosage regimen with oral medication during the vulnerable months when the depot drug is reaching a stable steady-state, (b) start the patient on a high or loading dose of depot neuroleptic during the first injections and decrease the dose during subsequent injections, and (c) use a shorter interinjection interval for the first injections.

The finding that FLU and FLUSO levels in the low-dose patients were at steady-state beginning at the time of randomisation was probably a result of the study design, as all patients were stabilised on FD before entry into the study. No attempt was made to 'wash out' the patients since studies have shown that FLU is detectable in the plasma for months after withdrawal from FD (Wistedt *et al*, 1982; Gitlin *et al*, 1988).

The finding that plasma levels of FLUSO are lower than levels of the parent compound in patients treated with FD is consistent with prior data from our group (Midha *et al*, 1987). In contrast, patients treated orally have significantly higher levels of the sulphoxide metabolite. For example, we treated eight schizophrenic patients with oral fluphenazine and measured their FLU and FLUSO levels after they reached steady-state (at two weeks). After these patients were clinically stabilised, they were subsequently converted to FD and had the same levels measured at three months, after they reached steady-state for the depot form. On oral fluphenazine, the patients had FLUSO levels approximately three-fold those of FLU, whereas after switching to FD, levels of the metabolite actually dropped below those of the parent compound. The reason for the difference in concentrations between the parent compound and metabolites is probably related to extensive metabolism during the first passage through gut and liver after oral administration. Since FD is administered parenterally, first-pass metabolism is avoided and the parent compound is more bioavailable (Marder *et al*, 1989).

Our data does not address clinical response at higher (for example >2.5 ng/ml) FLU levels. Our higher dose of 25 mg would be considered moderate by most clinicians and is unlikely to be severely toxic. Moreover, patients who had early evidence of toxic side-effects often left the study and were considered dropouts. Therefore, patients with toxic plasma levels would be unlikely to remain in our study beyond a relatively brief period. We did, however, have patients on 25 mg with plasma FLU levels as high as 4 ng/ml and 5 ng/ml, but these patients appeared to tolerate the drug well and did not demonstrate severe side-effects.

The relationship we found between plasma level and outcome does not lead to a simple conclusion about the best plasma level for maintenance therapy. Rates of psychotic exacerbation were relatively low above FLU levels of 0.8 ng/ml or 0.9 ng/ml, suggesting that this is a reasonable plasma level for maintenance. However, very few patients with levels above 1.2 ng/ml exacerbated, suggesting that if the clinician had given a priority to preventing relapse and was less concerned about side-effects, then this higher level might be preferable. On the other hand, patients with FLU plasma levels that are lower than 0.9 ng/ml may be on the linear part of the curve and would benefit from a dosage increase. Patients who received 25 mg of FD every two weeks had mean levels of about 1.4 ng/ml (see Table 2) and nearly all were on the flatter part of the curve. (Our mean levels are slightly higher than those reported by Glazer (1988) who found that 25 mg of FD every two weeks resulted in a mean concentration of 0.96 ng/ml as measured using RIA.) Patients receiving a 5 mg dose in our study had mean FLU levels of 0.6–0.7 ng/ml with standard deviations of 0.5–0.6 ng/ml, indicating that this dose led to a substantial number of patients having levels that rendered them vulnerable to psychotic exacerbations. These findings are consistent with our previous report (using the same population) which indicated that patients receiving 25 mg had very low rates of psychotic exacerbations, particularly in the final year of the study, whereas patients receiving 5 mg were at significantly greater risk. The measurement of plasma levels may, therefore, be most useful for clinicians who are treating patients with relatively low doses such as 5 mg, since relatively small adjustments at this level may have important effects on the amount of protection the patient is receiving from their drug.

Although patients had reached steady-state by 12 weeks, we did not find a statistically significant relationship between plasma level and clinical outcome until 26 weeks. This may have occurred because patients may need to remain at steady-state for some time – perhaps several weeks or months – if the drug is to provide adequate protection. Conceivably, patients who had just reached steady-state may have had their course of illness influenced by factors that were unravelling before 12 weeks.

These results are similar to those reported by Wistedt *et al* (1982) who studied levels of FLU and 7-hydroxy FLU (7-OH FLU) in patients who were either continued on FD or had a placebo substituted for their FD. They found that patients who relapsed on FD had a lower mean plasma level (0.92 ng/ml) than those who did not relapse (1.36 ng/ml). It is interesting to note that patients who relapsed in their study had higher levels than those who relapsed in ours. This may be related to a difference in analytical methods between the two studies. Their method had significant cross-reactivity of the antiserum with 7-OH FLU, a metabolite that we found in the plasma of patients treated with depot fluphenazine. As a result, the plasma levels they reported were actually the sum of levels of FLU and 7-OH FLU. Mavroidis *et al* (1984), on the other hand, found that patients receiving oral fluphenazine for the treatment of acute psychotic episodes responded well in the range of 0.13–0.70 ng/ml. In another study, Dysken *et al* (1981) reported that FLU levels above 0.2 ng/ml appeared to be effective. The lower levels in these later studies do not necessarily contradict our findings since the low levels of FLU they found may result from the extensive metabolism of oral fluphenazine. Conceivably, these patients may have had higher levels of FLU metabolites such as 7-PH FLU or fluphenazine-N-oxide which may have accounted for the effectiveness of the oral dose. Recent findings from our laboratory (Marder *et al*, 1989) indicate that patients treated with oral fluphenazine may have concentrations of these two metabolites that are higher than levels of the parent compound.

We also found that FLU plasma concentrations were correlated with akinesia at two, four, and 26 weeks following randomisation. (We previously reported this finding in a subset of this population (Marder *et al*, 1986).) This suggests a relatively weak relationship between higher plasma levels of fluphenazine and increased akinesia. We did not find a similar relationship between plasma concentrations and akathisia, dyskinesia, or retardation. The relationship between akinesia and plasma level during the early stage of the study, but not the later, would be explained if either of the following occurred: (a) there was a differential drop-out with patients with high plasma levels and akinesia leaving the study during the first six months; or (b) patients with higher plasma levels and akinesia developed a tolerance to this side-effect over time. We believe that the former explanation appears more likely since we have previously reported (Marder *et al*, 1987) that patients in this sample who dropped out tended to be those who were experiencing the most drug-induced dysphoria. However, we did not find in this sample that patients with higher plasma levels had a greater tendency to drop out.

Our clinical methods limit the generalisability of our findings. The relationship between outcome and plasma level that we found was only apparent for patients who could be well stabilised for six months or more. In addition, we did not study patients who appeared to require doses of FD higher than 25 mg every two weeks. Although we are unaware of any relevant data, it may be that higher FLU levels may be preferable during the period that follows an acute episode, but that levels as low as 0.8–1.0 ng/ml may be sufficient once patients have been stabilised for six months or more.

These results indicate that measuring plasma levels of FLU may be helpful to clinicians who are treating patients with FD. The usefulness of plasma levels is most apparent for those patients who are receiving relatively low doses. For these patients, a low plasma level (for example <0.6 ng/ml) may indicate that a dosage increase would increase the protection they receive from their medication. Nearly all patients receiving 25 mg of FD every two weeks had plasma levels that were associated with adequate protection, suggesting that measurement of plasma levels would not provide useful information for these individuals as long as they tolerated the 25 mg dose. If, however, side-effects at this dose were thought to cause dysphoria or compromise social adjustment, dosage reduction to achieve a plasma level in the range of 1.0 ng/ml would seem desirable. Even though there was no consistent relationship between EPS and plasma level across patients, side-effects in any one patient, at least in our experience, are always dose-dependent (Marder *et al*, 1987; Van Putten *et al*, 1988).

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Lithium Treatment and Prophylaxis in Unipolar Depression: A Meta-analysis

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Meta-analysis was used to establish the efficacy of lithium in acute treatment and prophylaxis of depressive illness from existing published clinical trials. Effect sizes were measured by the odds ratio using the Mantel–Haenszel method and the Pearson product-moment correlation coefficient. Some benefit from lithium, compared with other treatments, emerged from trials of acute treatment. Lithium was clearly superior to placebo in the acute treatment of bipolar depressed patients. In controlled studies of lithium prophylaxis over five months to three years, an impressive effect was found for lithium when compared with placebo. For uncontrolled studies there was a similar-sized effect, corresponding to an improvement in the rate of favourable outcome from 35% for placebo to 70% with lithium treatment. The comparison of lithium with other antidepressants in prophylaxis showed no conclusive advantage for lithium in unipolar illness. There is no reason to doubt the efficacy of lithium in the prophylaxis of unipolar depressive illness.

Two decades ago, it was possible to write that "the results obtained with lithium in depressive illness are almost uniformly bad" (Blackwell & Shepherd, 1968). By that time, there had arisen a rather unhelpful polarisation between proponents of lithium who were against controlled trials on ethical grounds (to withhold effective treatment from patients at risk of suicide was considered indefensible) and opponents who were prepared to doubt that any of the clinical observation and audit of apparent efficacy could be counted in lithium's favour until a controlled trial had taken place. Even now, the role of lithium in the acute treatment and prophylaxis of depressive illness remains more controversial than its other indications. Since its introduction into modern psychopharmacology by Cade (1949), a consensus has emerged that it is effective in the acute treatment of mania (Schou, 1959; Maggs, 1963; Davis & Fann, 1971; Lewis & Winokur, 1982) and in the prophylaxis of bipolar affective illness (Baastrup *et al*, 1970; Prien *et al*, 1973, 1984). In unipolar illness, however, there remains doubt, and lithium is not, for example, recognised for the prophylaxis of unipolar depressive illness by the Food and Drug Administration in the USA. Should we be convinced by the findings in relation to unipolar illness or remain sceptical?

Previous reviews of lithium's efficacy in unipolar depression have supported opposite positions. Several supported a positive effect in acute treatment (Schou, 1976; Murray, 1984; Doyal & Morton, 1984) and in prophylaxis (Schou, 1968; Davis, 1976; World Health Organization, 1989). Other authors have been negative (Prien, 1979; Baldessarini & Tohen, 1988). Most of these reviews have employed a narrative method in which studies were compared critically, on a qualitative basis. Using this approach, conclusions are based on which individual study is judged the best. Although Davis (1976) and Schou (1976) also attempted some statistical comparisons, as far as we are aware no author has previously used the techniques of meta-analysis to address the problem.

The aim of meta-analysis is to employ quantitative techniques to combine the results of different trials. A primary emphasis can be placed upon measuring effect size rather than simply 'significance' (see Gardner & Altman, 1990) for a recent plea to the psychiatric community to concentrate more on this aspect of statistical procedure). It is only by obtaining large numbers of patients that trials can convincingly measure the size of treatment effects and this is often feasible only by combining the results from several similar trials (Peto, 1978). While this is the basis for large prospective multicentre studies, it can also be applied to the retrospective analysis of a number of small trials that share a similar but not identical design. It is of course essential that the source trials are satisfactory: treatment should be randomised and outcome both well defined and evaluated blind to treatment. However, if these criteria are met, the statistical techniques for pooling data are relatively simple and deserve to be more widely known among psychiatrists and general physicians (Yusuf *et al*, 1985). In addition, trials of much less satisfactory design can also be quantitatively compared. This is of interest because if treatment effects in poorly controlled clinical studies are comparable with the better trials, it allows us to do greater justice to the clinical observations of an earlier generation of psychiatrists and to make more meaningful comparisons with real clinical conditions.

The present study illustrates the power of this method of review for assessing the value of lithium in the treatment and prophylaxis of unipolar depression. The magnitude of the treatment effects and the confidence we are justified in placing in them may be useful both in guiding the actions of clinicians and in better informing our patients.

Method

An effort was made to gather data from all published trials written in English comparing lithium to other treatments in depressive illness. This comprised a formal computer-aided search, together with an informal search through *Index Medicus*, previous reviews, quoted references in published studies and personal questioning of colleagues and personal correspondence with authors when particular details of interest were not available from the published material. This was not always possible in practice.

Controlled and uncontrolled studies were reviewed separately. Controlled studies were required to have a prospective or discontinuation design with random assignment of treatment, double-blind evaluation of outcome and serum lithium levels within the range 0.4–1.5 mmol/l. Uncontrolled studies were included if they had some kind of group comparison. The contrast could be based on different designs, for example, cross-over, mirror (pre- v. post-lithium intervals), retrospective, or historical controls.

No study satisfying these criteria was excluded *ad hoc*. The criteria for exclusion were: (a) only one publication from each study was included in the analysis, the most updated version being used when several papers were based on a single project (this was not uncommon), and (b) some controlled studies were not included because data were described in a way that did not permit quantification of the effect size (e.g. Bennie *et al*, 1983) or they had studied five or less unipolar patients (e.g. Melia, 1970; Cundall *et al*, 1972; Johnstone *et al*, 1988).

In classifying studies, terminology follows conventional usage (National Institute of Mental Health/National Institutes of Health, 1985): acute treatment refers to the use of drugs in a period that may be measured in weeks; prophylactic use is the use of a drug for months or years in an attempt to prevent depressive recurrences. A recurrence is a 'new' episode.

Statistical analysis of controlled studies

The significance and the magnitude of effects can be determined for categorical data from 2 × 2 tables, for example, treated/control × failure (no response or recurrence)/success (acute response or remained well). The Mantel–Haenszel method is the best known (Mantel & Haenszel, 1959), and lends itself particularly well to clinical studies. For the effect size, the odds ratio together with its associated confidence interval has been proposed (Yusuf *et al*, 1985). This approach was used for controlled studies (acute treatment and prophylaxis) and uncontrolled studies (acute treatment) in which categorical data were presented.

	failure	success	total
treated	a	b	$a+b$
control	c	d	$c+d$
total	$a+c$	$b+d$	n

The expected number of failures in the treated group (E) is given by:

$$E=\frac{(a+c)\times(a+b)}{n}$$

where $(a+c)$ = number of patients failing (or not improving) in the treated and control group
$(a+b)$ = number of patients in the treated group
n = total number of patients in the trial

Then, E is contrasted with the observed number of failures in the treated group (O). If treatment was wholly without effect, the quantity $(O-E)$ would differ only randomly from zero with variance (V) and standard error ($\sqrt{V}$) given by:

$$V=\frac{(a+c)\times(b+d)\times(c+d)\times(a+b)}{n^2\times(n-1)}$$

For i individual studies, the sum $\Sigma(O-E)_i$ would differ randomly from zero (with variance equal to the sum of individual variances, ΣV_i) if treatment were without effect. $\Sigma(O-E)_i$ will be negative if treatment is effective.

The odds of failure of patients treated with lithium relative to the odds of failure of patients receiving another treatment is given by $\exp((O-E)/V)$ with 95% confidence intervals $\pm\exp(1.96/\sqrt{V})$ (Yusuf *et al*, 1985). Each $(O-E)/V$ and the $\Sigma((O_i-E_i)/\sqrt{\Sigma V_i})$ is assumed to be normally distributed.

The χ^2 of heterogeneity is also reported. It tests whether between study differences are significant. It is given by the difference between the total χ^2 and the χ^2 of association with $n-1$ degrees of freedom where n is the number of studies, or:

$$\Sigma((O_i-E_i)^2/V_i)-(\Sigma(O_i-E_i))^2/\Sigma V_i \text{ in } i \text{ studies.}$$

Statistical analysis of uncontrolled studies

Uncontrolled prophylactic studies have tended to use a variety of methods to reach a statistical conclusion, and we have had to use declared P values to assess significance of effects and also to make estimates of effect size (Rosenthal, 1984). Assessment of significance levels requires the calculation of individual Z scores for each study from the one-tailed significance equivalent to that declared in the study (usually two-tailed). They are combined to derive an overall probability of effect $(\Sigma Z_i)/\sqrt{n}$, where Z is the score in standard deviation units corresponding to the level of significance (one-tailed) given in any study and n is the number of studies.

Effect size in these studies is calculated by transforming published statistics into a common measure such as Pearson's r. From this an estimate of effect size can be made by a transformation of r into Fisher's Z (Zr). The mean for n studies, $Z'r = (\Sigma Zr)/n$, is transformed back to r to summarise the overall effect size. The Pearson product–moment correlation coefficient r measures the degree of association between two variables, in this case lithium and good outcome. It is often preferred for uncontrolled prophylactic studies because it can be derived from the least published information. The studies were also compared to ensure that the pattern of results appears homogeneous. This was performed for both Z values ($\Sigma(Z - Z')^2$) and effect size ($\Sigma(N_j - 3)\ (Zr_i - Z'r)^2$) – both are distributed as χ^2 with $n - 1$ degrees of freedom, where n is the number of studies.

A common criticism of meta-analysis is the possible bias introduced by the failure to publish negative results, also known as the 'file-drawer' problem. To counter this potential bias, a fail-safe number can be estimated (Cooper, 1979). This is the number of studies with a null result that must be 'in the file drawers' to reduce the overall summed probability below the desired level of significance (by convention $P = 0.05$) (Rosenthal, 1984):

$$n = \frac{k(k(Z')^2 - 2.706)}{2.706} = \text{number of studies required to}$$

reverse conclusion

where k = number of studies, Z' = mean of Z.

Results

Acute treatment of depressive illness with lithium

Table 1 summarises the design of controlled and uncontrolled studies included in this review. It also describes the duration, admission and exclusion criteria. Most studies involved only unipolar patients. Where possible, the data from bipolars have been abstracted from the studies for separate analysis. Almost all the comparisons involving lithium and placebo were of cross-over design; studies comparing lithium with another antidepressant (imipramine, desipramine or tryptophan – see Table 2) were prospective. There have been no fully satisfactory prospective randomised comparisons with placebo that one might wish to see in evaluating any drug for its efficacy in depressive illness. The best available were Johnstone *et al* (1988), where the primary purpose was not the inclusion of unipolar patients, who were consequently too few in number to be informative, and Khan *et al* (1987), who employed minimisation (Taves, 1974) rather than simple randomisation in allocating treatment and for ethical reasons allowed patients to drop out on clinical grounds. The criteria for this were not defined clearly in advance, but the drop-outs dominated the pattern of response and provided the only unambiguous way of comparing lithium and placebo; the advantage from lithium treatment compared with placebo was not statistically discernible (Table 2).

Table 2 summarises the findings in detail. The prospective studies comparing lithium with placebo, desipramine, imipramine or tryptophan showed a modest advantage for lithium which just reaches statistical significance for the comparison with active treatments. No individual placebo cross-over study showed a statistically significant effect favouring an antidepressant action for lithium. Overall patient numbers are small and the results far from conclusive.

Table 1
Studies of the acute treatment of unipolar and bipolar[1] depression with lithium

Study	Duration	Admission criteria	Exclusion	Drop-outs: ill/other
Controlled				
Mendels *et al* (1972)	3 weeks	Hamilton score >15	Not described	Nil/nil
Watanabe *et al* (1975)	3 weeks	"affective disorder"	Physical only	6/9
Worrall *et al* (1979)	3 weeks	>2 previous episodes	Not described	2/1
Khan (1981)	3 weeks	>3 previous episodes	Severe depression	3/2
Khan *et al* (1987)	6 weeks	>1 previous episode Hamilton score >17	Suicide risk	6/8
Uncontrolled				
Goodwin *et al* (1972)	Lithium 2 weeks, placebo 6 days	In-patient, symptom list	Not described	Nil/nil
Noyes *et al* (1974)	Lithium 2 weeks, placebo 4 days	>1 previous episode, Symptom list	Reactivity, hysterical personality	Nil/nil
Baron *et al* (1975)[1]	Lithium 2 weeks, placebo 2 weeks	Episode >4 weeks Feighner positive	Not described	Nil/nil
Mendels (1976)[1]	Lithium 3 weeks, placebo 1–3 weeks	Severely ill, Hamilton score >28	Not described	Nil/nil

Controlled studies were prospective and randomised, with double-blind evaluation. Only Khan *et al* (1987) was placebo controlled; the others compared lithium with another antidepressant. The design used in uncontrolled studies of lithium v. placebo was cross-over, with either single-blind (only Noyes *et al*, 1974) or double-blind evaluation; in most of them the process of randomisation is not clearly stated. In the uncontrolled trials the duration of the lithium period was usually greater than the placebo period. In Watanabe *et al* (1975) 25% of patients withdrew from the trial.

1. Only the studies by Baron *et al* (1975) and Mendels (1976) give information for bipolar patients. In Mendels *et al* (1972) unipolar and bipolar groups could not be separated and only the first phase of the study has been included (cross-over phase omitted).

Table 2
Lithium v. other treatments in acute depression

Study	Lithium		Comparison treatment		Calculations				
	not improved	improved	not improved	improved	$(O-E)$	variance $(O-E)$	P	odds ratio	95% CI
Unipolar depression: controlled									
Lithium × placebo									
Khan *et al* (1987)	6	8	8	5	−1.3	1.7	NS	0.5	0.1–2.2
Lithium × other antidepressants									
Mendels *et al* (1972)									
(desipramine)	3	9	6	6	−1.5	1.5	NS	0.4	0–1.8
Watanabe *et al* (1975)									
(imipramine)	4	22	3	16	0.0	1.5	NS	1.0	0.2–4.9
Worrall *et al* (1979)									
(imipramine or tryptophan)	9	13	19	8	−3.6	3.0	0.04	0.3	0.1–1.0
Khan (1981)									
(imipramine)	2	13	2	13	0	0.9	NS	1.0	0.1–7.9
Total pooled data	18	57	30	43	−5.1	6.9	0.05	0.5	0.2–1.0
Uncontrolled, cross-over									
Lithium × placebo									
Goodwin *et al* (1972)	8	4	10	2	−1.0	1.2	NS	0.4	0.1–2.6
Noyes *et al* (1974)	9	7	5	2	−0.7	1.2	NS	0.5	0.1–3.2
Baron *et al* (1975)	7	3	8	2	−0.5	1.0	NS	0.6	0.2–3.6
Mendels (1976)	4	4	1	3	0.7	0.7	NS	2.5	0.2–26.5
Total pooled data	28	18	24	9	−1.6	4.1	NS	0.7	0.2–1.8
Bipolar depression									
Lithium × placebo									
Baron *et al* (1975)	1	7	5	3	−2.0	1.0	<0.04	0.3	0.1–1.0
Mendels (1976)	4	9	6	3	−1.9	1.4	NS	0.3	0.1–1.3
Total pooled data	5	16	11	9	−3.9	2.4	<0.01	0.2	0.1–0.7

Lithium was compared with other antidepressants in trials using only unipolar patients. Lithium was compared with placebo in cross-over trials including unipolar and bipolar depressed patients. $(O-E)$ is the difference between the observed and expected number of failures in the lithium group. Variance (V) is given as described in Method, P is the two-tailed probability corresponding to each normal deviate which is given by $(O-E)/\sqrt{V}$. Outcome was designated in Watanabe *et al* (1975) as improved group = fairly to markedly effective, not improved group = ineffective or worse and in Noyes *et al* (1974) as improved group = recovered, marked or moderate, not improved group = slight or worse.

Odds ratios of < 1.0 favour lithium, > 1.0 give advantage to the other treatment. Lithium v. other antidepressants in controlled studies of unipolar illness show a just significant advantage to lithium; lithium v. placebo in cross-over studies of unipolar illness showed no statistically significant effect; lithium v. placebo in bipolar depressed patients showed an advantage to lithium. No χ^2 of heterogeneity was significant for individual groups of studies.

Effect size was calculated as the odds ratio (with 95% confidence intervals) for each study individually and as a pooled summary statistic (Table 2). Largely because of the study by Worrall *et al* (1979) in which the comparison treatment was tryptophan or imipramine, lithium is just superior to other treatments. However, all studies tend to show an advantage to lithium treatment and hence the studies appear homogeneous ($\chi^2 = 2.45$). It will be obvious that the confidence interval is wide and extends almost to an odds ratio of 1 (or no difference).

The result of the comparison, lithium v. placebo in *bipolar depressed* patients, does support a more statistically significant effect. Overall effect size is not tightly specified, however, because the confidence interval remains wide.

Prophylaxis of depressive illness with lithium

Table 3 summarises the design and clinical characteristics of the controlled and uncontrolled studies of the prophylaxis of unipolar depression with lithium. Ten studies are of randomised design and examine follow-up intervals of five months to three years. They are further analysed in Table 4, which summarises outcome in terms of treatment success or failure. Most trials of lithium v. placebo have shown a statistically significant benefit from lithium. However, the largest, by Prien *et al* (1984), showed no statistically significant effect. The particular advantage of the analysis presented in Table 4 is that the effect size in this study is shown to be compatible with that of other studies and to favour lithium treatment. However, because the rates of recurrence in both groups were high, the variance and hence the confidence interval were increased.

The summary statistics for the pooled data are powerfully in favour of a benefit from lithium compared with placebo (Table 4). The pooled odds ratio when lithium was compared with placebo was 0.2 (95% CI 0.1–0.4). In other words, lithium prophylaxis reduced the odds of recurrence over about one year (the average duration of the trials)

Table 3
Characteristics of studies in the prophylaxis of unipolar depression with lithium

Study	Design	Duration	Admission criteria	Exclusion criteria	Drop-outs Li/other
Controlled					
Baastrup *et al* (1970)	Discontinuation	5 months	On lithium >1 year	Schizoaffective	1/4
Coppen *et al* (1971)	Prospective	Up to 26.1 months	Frequent episodes	Not described	?/?
Hullin *et al* (1972)	Discontinuation	6 months	No admission previous 2 years, on lithium	Physical disorders	?/?
Prien *et al* (1973)	Prospective	5–24 months	Frequent episodes	Severe illnesses, age >60 years	12/11 (imipramine)/ 20 (placebo)
Fieve *et al* (1976)	Prospective	Mean for lithium 20.5 months, mean placebo 9 months	Feighner positive, frequent episodes	Hypomania	2/3
Coppen *et al* (1976)	Prospective	12 months	On lithium >1 year, >3 previous episodes	Not described	5/9
Coppen *et al* (1978)	Prospective	12 months	>3 previous episodes	Severe psychiatric and physical illnesses	5/8
Kane *et al* (1982)	Prospective	Mean 11 months	RDC[1], frequent episodes, euthymia 6 months	Other medication <18 years, >65 years	?/?
Glen *et al* (1984)					
(Glen I)	Prospective	Up to 36 months	RDC, >1 episode	Physical illnesses, <25 years >65 years	1/3
(Glen II)	Prospective	Up to 36 months	RDC, first episode		0/1 (amitriptyline)/ 0(placebo)
Prien *et al* (1984)	Prospective	24 months	RDC, frequent episodes, rating scales scores	Other psychiatric and physical illnesses, <21 years, >60 years	?/?/?
Uncontrolled					
Baastrup & Schou (1967)	Mirror	Before = 6.5 years on lithium = 1.5 years	Frequent episodes, on lithium>1 year	Not described	Nil
Angst *et al* (1970)	Mirror	Before, mean 9.1 months, on lithium mean 9.1 months	Frequent episodes	Not described	Nil
Persson (1972)	Historical controls	Before, 2 years; on lithium 2 years	>1 episode	Not described	12
Lepkifker *et al* (1985)	Retrospective	1–15 years	>3 previous episodes	Various	15
Smigan *et al* (1985)	Mirror	Mean 27.3 months	On lithium, frequent episodes,	Various	10
Bouman *et al* (1986)	Retrospective	Before, mean 7.8 years; on lithium, mean 64.5 months	Feighner positive, frequent episodes	Not described	Nil
Souza *et al* (1990)	Retrospective discontinuation	2 years	DSM-III-R	Other psychiatric medication	Nil

Glen I refers to the study of Glen *et al* (1984) comparing lithium and amitriptyline in recurrent unipolar depression; Glen II was the other half of the study in which first-episode depressives were treated with lithium, amitriptyline or placebo. Mirror design means that patients were studied before and after introduction of lithium; in many of these trials the length of the lithium period was different from the placebo period. In Hullin *et al* (1972) unipolar and bipolar groups could not be separated. In Prien *et al* (1973) only the second phase is reported (5–24 months); the first phase (1–4 months) was omitted but showed similar results.

1. Research Diagnostic Criteria.

Table 4

Study	Lithium		Comparison treatment		Calculations				
	not improved	improved	not improved	improved	$(O-E)$	variance $(O-E)$	P	odds ratio	95% CI
Lithium × placebo									
Baastrup *et al* (1970)	0	17	9	8	−4.5	1.7	<0.0006	0.1	0–0.3
Coppen *et al* (1971)	1	10	12	3	−4.5	1.7	<0.0004	0.1	0–0.3
Hullin *et al* (1972)	1	17	6	12	−2.5	1.5	<0.03	0.1	0–0.9
Prien *et al* (1973)	9	13	11	2	−3.5	2.1	<0.01	0.1	0–0.7
Fieve *et al* (1976)	8	6	9	5	−0.5	1.7	NS	0.7	0.2–3.3
Kane *et al* (1982)	2	5	6	0	−2.3	0.8	<0.01	0.1	0–0.5
Glen *et al* (1984)	5	6	8	1	−2.1	1.2	<0.04	0.1	0–0.7
Prien *et al* (1984)	21	16	24	10	−2.4	4.2	NS	0.6	0.3–1.4
Total pooled data	47	90	85	41	−22.3	14.8	<0.00006	0.2	0.1–0.4
Lithium × other antidepressants									
Prien *et al* (1973)	9	13	6	15	1.3	2.5	NS	1.3	0.4–4.0
Coppen *et al* (1976)	3	9	6	2	−2.4	1.2	<0.03	0.2	0.1–0.9
Coppen *et al* (1978)	0	15	7	6	−3.8	1.3	<0.001	0.1	0–0.5
Kane *et al* (1982)	2	5	5	1	−1.8	0.9	<0.04	0.2	0–1.0
Glen *et al* (1984) (I)	32	14	39	16	−0.3	5.3	NS	0.9	0.4–2.2
Glen *et al* (1984) (II)	5	6	4	3	−0.5	1.1	NS	0.7	0.1–4.0
Prien *et al* (1984)	21	16	16	22	2.7	4.7	NS	1.8	0.7–4.3
Total pooled data	72	78	83	65	−4.7	17.1	NS	0.7	0.5–1.2
Lithium × lithium + imipramine									
Kane *et al* (1982)	2	5	1	7	0.6	0.6	NS	2.5	0.2–29.5
Prien *et al* (1984)	21	16	12	25	4.5	4.6	<0.03	2.6	1.0–6.5
Total pooled data	23	21	13	32	5.1	5.3	<0.02	2.6	1.1–6.1

The pooled results for the comparison lithium v. placebo indicates a powerful treatment effect for lithium ($P<0.00006$) while the result obtained with the comparison lithium v. other antidepressants was not significant. Only two studies compared lithium with the combination lithium + imipramine and the pooled result favoured the combination ($P<0.02$). Glen I data are from patients with more than one previous episode, Glen II data are from patients with one depressive episode. χ^2 of heterogeneity was found significant in lithium v. other antidepressant treatment ($\chi^2=19.1$, d.f. = 6, $P<0.01$), where different trials showed different results.

by 78% (95% CI 87–64%). This result corresponds to the sum for $O-E$ of -22.3, suggesting about 45 recurrences had been avoided with the use of lithium (out of a total of 137 patients treated; there were 126 untreated controls). This summary combines data from discontinuation studies with that from randomised prospective treatment (Table 3). If discontinuation studies are excluded, the effect size is 0.26 (95% CI 0.2–0.5) and so remains essentially unchanged.

In contrast, lithium is not demonstrably superior to antidepressant treatment in preventing recurrence. The pooled odds ratio of the comparison lithium v. other antidepressants was 0.7 (95% CI 0.5–1.2). The confidence

Table 5
Prophylaxis with lithium in unipolar depression: uncontrolled studies

Study	P	Z	n	r	Zr
Baastrup & Schou (1967)	<0.0005	3.3	22	0.70	0.86
Angst *et al* (1970)	0.0005	3.3	58	0.40	0.42
Persson (1972)	0.01	2.3	32	0.40	0.42
Lepkifker *et al* (1985)	0.001	3.1	33	0.54	0.60
Smigan *et al* (1985)	0.37	0.3	19	0.07	0.07
Bouman *et al* (1986)	0.26	0.6	20	0.13	0.13
Souza *et al* (1990)	0.001	3.1	40	0.49	0.53
Total		16.0			3.03
Mean		2.3		0.41	0.43

Pearson correlation coefficients (r) for the uncontrolled studies were homogeneous, and the overall correlation was $r=0.41$. P is the reported level of significance (one-tailed). Z is the normal deviate (one-tailed) corresponding to each P. n is the number of patients studied. r is Pearson product–moment correlation coefficient, given by $Z/\sqrt{n}$. Zr is the transformation of r in Fisher's Z where $Zr=1/2\log_e((1+r)/(1-r))$. The 'mean' value for r (given in parenthesis) is derived from the mean for Zr.

interval leaves appreciable room for debate about the relative efficacy. Some antidepressants may be less effective than others (e.g. mianserin, see Table 4). Lithium alone has been compared with lithium plus imipramine in some studies; the results are wholly inclusive (Table 4).

Table 5 summarises the findings of the uncontrolled prophylactic studies. As explained under 'Method', the wide differences in mode of data analysis and presentation make an approach based on the Mantel-Haenszel method impracticable. Instead, following Rosenthal (1984), we have compared and combined significance levels and effect sizes estimated from the P values declared in each trial. Significance levels differ significantly, indicating study heterogeneity ($\chi^2 = 11.43$, d.f. 6, $P < 0.05$), but all support a similar positive treatment effect from lithium. Thus the combination of probabilities was highly significant ($Z = 6.5$). The combined effect size was found to be in the medium range ($r = 0.41$). The combined effect size of the controlled studies expressed in the same terms was $r = 0.42$. These values of r can also be understood in terms of proportional outcome (Rosenthal, 1984). An r value of 0.4 corresponds to an improvement in positive outcome of from 30% to 70%.

The number of additional studies that would be necessary to reverse the main findings illustrated in this meta-analysis necessarily vary according to the effect size obtained in each comparison. Only one statistically non-significant study need be published to invalidate both the conclusion that lithium is more effective than other treatments in unipolar depressed patients, and the finding that lithium plus imipramine is superior to lithium in unipolar depression. Three negative studies could reverse lithium's positive treatment effect in depressed bipolars. However, for the strongest effect, lithium v. placebo in the prophylaxis of unipolar illness, 108 'negative' studies would be needed to invalidate the conclusion currently favouring lithium. It should be appreciated that a negative study for these purposes need not show an opposite effect to that currently seen; assuming random treatment effects, some would favour a treatment effect, some not.

Discussion

Acute treatment with lithium alone in unipolar depression has rarely been subject to satisfactory evaluation and too few patients have been entered into satisfactory trials. Comparison with placebo, in particular, allows substantial grounds for doubts as to the efficacy of lithium alone in unipolar patients. Only the study of Khan *et al* (1987) is of prospective design. However, there is also a strongly positive finding by Worrall *et al* (1979) and Worrall (1986) has subsequently argued that patients treated with tryptophan should be seen as receiving an antidepressant of limited efficacy. We have preferred to combine Worrall *et al*'s data for imipramine and tryptophan rather than treating tryptophan as a placebo. Indeed, the best evidence in favour of lithium's efficacy comes from several trials comparing lithium with other established antidepressant treatments; these reveal a marginal advantage or at worst equality for lithium. However, the confidence intervals listed in Table 2 show that we simply cannot be confident about how effective lithium is compared either with placebo or other antidepressants. There does appear to be an acute treatment effect in bipolar patients who are depressed and such patients ought to be excluded as far as possible from studies of unipolar patients.

It may be objected that the use of a binary outcome scale in assessing the effects of acute treatment is too arbitrary and may tend to reduce the significance of comparisons based on continuous changes in a rating scale score. Inevitably, trying to transform continuous quantitative data, such as degrees of clinical improvement into some sort of qualitative classification (e.g. not improved in treatment studies) is more arbitrary than a classification where outcome is either death or survival. However, this may magnify treatment effects as often as it diminishes them. The advantage of the methods employed here are that they are quite conservative and binary assessments probably reflect clinical decision making.

There are also methodological short-comings in many of these studies; duration of treatment may have been too short (e.g. Goodwin *et al*, 1972; Baron *et al*, 1975), and the analysis may be based on the outcome of the patients who remained in the trial, even when an appreciable number of patients dropped out (Watanabe *et al*, 1975; Khan, 1981). These objections serve to further qualify our uncertainty, but they cannot much increase it.

Outcome in the controlled studies of prophylaxis was expressed in terms of recurrence. This meant different things in different studies: some used readmission to hospital as the criterion of failure (Hullin *et al*, 1972) while others used introduction of other treatment such as electroconvulsive therapy or antidepressants (Fieve *et al*, 1976) or a change in an index of morbidity (Coppen *et al*, 1976; Kane *et al*, 1982; Prien *et al*, 1984). However, the findings were remarkably homogeneous. Across different studies, be it those examining discontinuation of lithium in patients who may have been selected lithium responders, or those in which lithium was being started prospectively, the effect size was large and consistently in favour of lithium compared with placebo. Follow-up was often short, and may sometimes have included patients who were relapsing rather than recurring, but there is overall, no reason to doubt the efficacy of lithium as an active compound v. placebo in unipolar illness. Even the largest of the 'negative' studies, by Prien *et al* (1984), is not in conflict with the results from other studies when viewed in terms of effect size and confidence interval. This, in a nutshell, illustrates the difference in emphasis between a statistical analysis based on significance levels compared with one based on effect size. Further, the difference is not a trivial one, because the analyses lead to opposite conclusions: that lithium is ineffective (because 'not significant') or that it may be effective but the confidence interval is too great to allow certainty. It appears self-evident which is the most clinically useful.

The magnitude of the effect of lithium in controlled studies of prophylaxis appears fully compatible with the observations in uncontrolled studies that in the past have received so much criticism, for example those by Baastrup *et al* (1967) and Angst *et al* (1970).

The efficacy of lithium in comparison with other antidepressants provides less ground for confidence. The pooled effect suggests a tendency for lithium to be more effective, and individual trials strongly suggested this (e.g. lithium v. mianserin (Coppen *et al*, 1976). However, comparison with conventional tricyclic drugs tended to show no advantage for lithium, albeit with wide margins of error. The simplest conclusion is that we do not know whether the choice of lithium in recurrent unipolar depression is better prophylaxis than amitriptyline or imipramine.

There were weaknesses in the trials of prophylaxis. These included:

(a) previous use of lithium – a bias is introduced if it is already known that these patients are good lithium responders (Baastrup *et al*, 1970; Coppen *et al*, 1976)

(b) blindness – in Coppen *et al* (1971) and Prien *et al* (1973) the raters were blind but the treating doctors were not, and many decisions regarding the treatment of the patients were taken by the doctor in charge

(c) withdrawal – a variable number of patients withdrew from trials and they were often excluded from the statistical analysis (see Table 3).

(d) different follow-up periods both between studies (from five months to three years) and even within studies (Fieve *et al*, 1976; Kane *et al*, 1982); the only advantage of the relatively short duration of these trials was to reduce as a possible confounding problem the worsening prognosis that may develop with disease progression (Zis & Goodwin, 1979).

No historical survey of clinical trials in depressive illness is complete without an acknowledgement of diagnostic uncertainty. The classification of patients with affective disorders into bipolar and unipolar groups proposed by Leonhard *et al* (1962), Perris (1966) and Winokur (1973) was slow to receive wide acceptance and a failure always to make this distinction may have flawed some of the earlier uncontrolled trials. The better-controlled trials appear to have been more careful in this regard. Some recurrent unipolar patients may also become bipolar, given time. Indeed, it could even be argued that a response to lithium may occur because patients are 'really' bipolar. This is, of course, unimportant from a practical point of view and, equally, in the absence of an independent validating test for bipolar disease, difficult to address scientifically. The criteria for depressive illness have also been refined over the years. However, the diagnosis of a major depressive episode, recurrent, as in DSM-III-R (American Psychiatric Association, 1987), is not especially exacting and has never attracted the same controversy as classification of the psychoses. The major positive conclusions of this review appear to be based primarily on findings in patients where diagnosis was broadly acceptable.

In summary, the existing literature strongly supports the value of lithium in prophylaxis of recurrent unipolar depressive illness. The odds of falling ill compared with staying well are improved by lithium treatment to between 0.3 and 0.7 of what they are with placebo. This effect size is clinically significant because rates of recurrence in unipolar illness can be high. These effects are identical in magnitude with those from studies that have examined apparent clinical response in non-random designs. However, no advantage can be claimed for lithium over other antidepressants particularly the older tricyclic drugs, and the value of lithium alone in acute treatment remains uncertain. The uncertainty that remains is the result of remarkably few patients ever having been randomised in trials of acute lithium treatment.

Finally, there is a need for perspective in the evaluation of clinical trials and their comparison with uncontrolled clinical studies and data from audit. The techniques employed here offer considerable advantages and deserve to be much better known. It is difficult, given the advantage of hindsight, not to reach the conclusion that lithium's value in prophylaxis of depression was clinically apparent to the workers who first employed it and their quantitative estimates of its value from uncontrolled studies were not exaggerated. An argument about the quantities rather than the qualities exhibited by the research might have been more fruitful at the time. There is certainly every reason to use quantitative methods to address such controversies now and in the future.

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Social Influences on the Course of Anxious and Depressive Disorders in School-Age Children

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In a follow-up study of 49 children and adolescents with anxious or depressive disorders up to 50% had not recovered. In the 12 months preceding onset there were no social factors which predicted recovery at follow-up. Between onset and follow-up the children were less likely to be exposed to undesirable life events, and significant improvements in maternal confiding relationships were reported. Neither of these improvements predicted the level of recovery at follow-up. Poor recovery is best predicted by moderate to poor friendships after the onset of disorder, particularly for those with a diagnosis of depression. Further confirmation is provided that direct interviewing of children by trained personnel using semistructured schedules is a valid method for determining mental symptoms and perception of recent friendships.

Recent longitudinal studies have indicated that the outcome for depression in young people is worse than previously considered (Kovacs *et al*, 1984*a*,*b*; Eastgate & Gilmour, 1984; McGee & Williams, 1988). Chronic relapsing depressive conditions lasting more than two years have been described (Keller *et al*, 1988; McGee & Williams, 1988). Even in disorders of short duration, the probability of remaining depressed after one and two years is approximately 30% and 10% respectively (Kovacs *et al*, 1984*a*,*b*; McGee & Williams, 1988). Follow-up studies of young adults who reported depressive symptoms as adolescents indicate they are likely to experience further psychiatric disability, more unemployment, divorce, and educational failure than those who were not depressed during adolescence (Eastgate & Gilmour, 1984; Kandel & Davis, 1982). These findings indicate that children and adolescents with major depression are at high risk from relapse, and some experience a chronic course which may act as a forerunner of social impairment in adult life.

The mechanisms related to poor outcome remain unclear. Studies of adult depression have shown that social factors influence the course of disorder. For example, undesirable life events after the onset of symptoms decrease the probability of a good outcome from treatment (Murphy, 1983; Rowan *et al*, 1982; Giel *et al*, 1978; Miller *et al*, 1987). By contrast, desirable life events following diagnosis have been found to aid treatment and improve outcome (Paykel & Tanner, 1976; Tennant *et al*, 1981). No such studies have been reported for depression or anxiety in children or adolescents. This paper reports a follow-up study of a clinic population of anxious and depressed children.

Current evidence suggests that different diagnoses coexist in developmental psychopathology (Fleming *et al*, 1989). For example, in some 40% of depressive disorders there are sufficient anxiety symptoms to meet criteria for anxiety disorders (Kovacs *et al*, 1989). Furthermore, Kovacs and colleagues demonstrated that anxiety disorders preceded depression in some two-thirds of cases, suggesting either that anxious and depressive presentations reflect different evolutionary periods of the same disorder, or that anxiety predisposes to depression in some as yet unspecified way. These findings support the assumptions in this research that anxious and depressive subgroups of emotional disorder should be treated as one group and comparisons between subgroups should be carried out to determine points of rarity and contact in their onset, course and outcome.

The purpose of the study was threefold:

(a) to investigate the general outcome of anxiety and depression in children and adolescents of school age
(b) to determine the degree of agreement between children, their mothers and psychiatrists on the assessment of recovery at follow-up
(c) to evaluate the contribution of social factors in the child's recovery by considering (i) factors preceding onset of disorder and (ii) factors after diagnosis.

Method

A repeat-measure design was used for the follow-up study. Full details of patient selection, classification and measurement have been published elsewhere (Goodyer *et al*, 1988, 1989). Patients were selected from a cross-sectional prospective study investigating the influence of social and family factors on the onset of anxiety and depression in school-age children.

Psychiatric cases were obtained from the clinics of the Manchester University Department of Child and Adolescent Psychiatry within the Royal Manchester Children's and Prestwich Hospitals.

Inclusion criteria for the study were:

(a) age between 7 and 16 years old
(b) not suffering from mental handicap
(c) living with mothers or mother surrogates for at least two years before referral
(d) mothers or mother surrogates free of recent psychoses or serious medical conditions likely to impair their ability to take part in research interview
(e) onset of disorder within the last 14 months, so that retrospective recall of recent life-event information was no longer than 26 months
(f) criteria met for emotional disorder described in the appendix.

Onset of disorder was defined as (i) the appearance of new symptoms or (ii) a marked and identifiable change in the frequency, duration and quality of signs and symptoms which resulted in referral.

All cases reported here were collected between August 1984 and October 1985. Of 1100 children referred to the services participating in the study, 121 met the criteria for inclusion and 115 (95%) of these agreed to participate. Thus, new-onset emotional disorders in school-age children represented approximately 10% of all referrals and approximately 50% of all forms (acute and chronic) of emotional disorders in school-age children who attended the clinics over the study period.

The first 100 cases were classified into three groups in terms of onset of disorder as follows:

(a) no evidence of signs and symptoms before onset ($n = 38$)
(b) vague distress which did not affect the child's life, developing into definable new signs and symptoms resulting in referral – onset was taken at the point of new symptoms being reported ($n = 32$)
(c) vague distress whose degree, frequency and quality had altered resulting in referral ($n = 30$).

The emergent symptoms prompted referral because previously they had not been causing difficulties for the child or altering his/her everyday living but were now doing so. Onset was taken as the point where symptoms were reported as emergent.

Of these first 100 patients in the cross-sectional study 32 were classified as predominantly depressed emotional disorder, meeting DSM-III (American Psychiatric Association, 1980) criteria for major depressive episode. These subjects were identified as the index group for follow-up. Four were untraceable. The remaining 28 were matched for age and sex with 28 children classified as anxious (from the remaining 68 of the total patient sample). These latter cases were heterogeneous according to DSM-III criteria. Eighteen were classified as separation anxiety disorder, eight as overanxious disorder, and two as avoidant disorder.

These 56 patients formed the follow-up group. Of these, 49 (88%) (28 depressed, 21 anxious) agreed to be interviewed.

Measures

Only patients with a new-onset disorder of less than 14 months were entered into the original study. Measures of recent undesirable life events, social achievements, friendship difficulties, maternal confiding relationships and maternal distress which had been taken in the cross-sectional study were repeated by new interviewers blind to the original interviews. The methods of data collection and forms of measurement, including their reliability and validity, have been reported in detail in previous publications (Goodyer *et al*, 1985, 1988, 1989, 1990). The principles and procedure for each measure and rating are described in the appendix.

All mothers and children were interviewed at home – a total of 98 interviews.

One of two interviewers (EG and JG, both psychiatrists) carried out the interviews with the children using a short children's interview schedule concerning mood and behaviour sufficient to determine the presence or absence of anxious or depressive disorders. The schedule has been used in previous research and contains items from the Edinburgh depression inventory (but used in interview form) for young people together with relevant items from the Isle of Wight Children's Interview (Birleson, 1981; Foreman & Goodyer, 1988; Rutter & Graham, 1968). The interview used a global method of scoring on a three-point scale of present, partial (symptoms reported but overall below a threshold of 'caseness'), or no psychiatric disorder. The interviewers had previously demonstrated 90% agreement on rating the presence or absence of psychiatric disorder in 12 children in the child psychiatry department, each psychiatrist having interviewed six children while both rated concurrently.

The children's interview was carried out without mothers being present. Children's present mental state was assessed first, followed by their social adjustment using the index of friendships interview.

Life events, social achievements and maternal confiding relations were collected from the mother. Mothers then completed the 'index of friendships' interview to obtain their perception of their child's social adjustment since discharge, followed by mental state questions relating to how the child was at present. Finally, mothers were asked to rate their child's recovery on the three-point scale: (a) recovered, (b) partially recovered, (3) not recovered (see below for criteria).

Thus three outcome measures were obtained: mothers', children's, and interviewers'. Mothers' and children's ratings were derived from their information about mental state from their respective interviews. Interviewers derived a composite judgement from both mother and child interviews. A three-point scale was used:

(a) recovered: no mental state abnormalities
(b) partially recovered: overt symptoms but below the level of 'caseness'
(c) not recovered: symptoms meeting DSM-III criteria for anxious or depressive disorders.

In view of the small sample size and to maintain consistency with the original entry criteria of the cross-sectional study, subjects were divided into anxiety-dominant or depressive-dominant disorders.

Statistical methods

Results are analysed using non-parametric (McNemar's test, which takes into account chance agreements), χ^2 and logistic regression methods where appropriate. For the logistic regression analyses the subjects were treated as independent and we analysed the anxiety/depression dependence on the covariates (including age and sex). This technique determines the best fit of the data and calculates the log odds of the probability of being anxious or depressed. The statistic reported is the scaled deviance, which approximates the χ^2 when the fitted model is correct. The small sample size imposes constraints on the interpretation of any findings, which must be taken as conservative and preliminary.

General linear interaction models take into account sample sizes in computing the standard errors of the parameter estimates; it is the comparison of these parameter estimates with their standard error that is the basis for assessing whether or not the corresponding factors are significant. (See Healy (1989) for a full discussion of Glim and chapter 7 in particular for a full explanation of the above statistical argument. See also Fleiss *et al* (1986) for an account of the use of logistic regression analysis in psychiatric research.)

Results

There were 26 girls and 23 boys. At first assessment, mean age was 13 years 1 month (s.d. 27 months). Eight children (two anxious and six depressed) had not accepted treatment and been discharged from out-patient care by their families against psychiatric advice. At the second assessment the mean age was 14 years 3 months (s.d. 30 months). The length of recall for social data since discharge ranged widely, therefore time since discharge was treated as a further independent variable for analysis of results.

Recovery at follow-up

Table 1 shows the proportions of subjects dichotomised as not recovered (including partially recovered and recovered). The children appeared significantly more optimistic than psychiatrists (McNemar's test, $P<0.05$). No significant differences were found between mothers and children or mothers and psychiatrists. Anxious children appear to account for most of the differences, with proportion judged recovered ranging from 86% by the children, 62% by their mothers and 43% by the psychiatrists. By contrast, for depressed children, 43% were rated as recovered by the children, 53% by their mothers and 50% by the psychiatrists. There was, however, only 60% agreement between the three sources on the three classifications of recovery.

Table 1
Child's, mother's and psychiatrist's judgements of recovery for 49 anxious and depressed children

	Child		Psychiatrist	
	Recovered		Recovered	
	no[1]	yes	no[1]	yes
Mother				
Recovered				
no[1]	14	7	18	3
yes	5	23	8	20
Child				
Recovered				
no[1]	–	–	17	2
yes	–	–	9	21

Significant disagreement only found between child and psychiatrist information (two out of 11 discordant pairs) ($P<0.05$).
No significant disagreement between mother and child, or mother and interviewer information.
1. Includes partial recovery.

The association between social factors before and after onset of disorder

Table 2 cross-tabulates social factors before onset of disorder and after presentation. The overall proportions of children and mothers reporting adversities and achievements were not significantly different before and after for the factors friendships, maternal distress (reflected in the Rutter Malaise score) and social achievement. Mothers do, however, report significant improvement in their own confiding relations at follow-up (McNemar's test, $P<0.01$). In addition they report that significantly fewer children have been exposed to one or more undesirable life events since presentation (McNemar's test, $P<0.01$).

Influence of social adversity on recovery

The above findings confirm a substantial difference between informants' reports of the quality of recovery. The relationship between social factors and recovery may therefore vary according to whose view of recovery (mother,

Table 2
Social factors before onset of disorder and after presentation in children

Before onset	After presentation	
Children's reports		
Their own friendships	moderate/poor	good
moderate/poor	4	7
good	4	34
Their own achievements	none	one or more
none	11	14
one or more	8	16
Mothers' reports		
Their own confiding relationships[1]	poor	moderate/good
poor	6	28
moderate/good	6	9
Their Rutter Malaise scores	positive	negative
positive	12	6
negative	6	25
Their children's undesirable life events[1]	none	one or more
none	13	4
one or more	23	9

1. Significant improvement at the 1% level.

child or interviewer) is taken. If agreements between respondents are found for social factors and the quality of recovery then this likely to indicate meaningful effects which are not simply a result of respondent bias or confounding of the interview method.

Three logistic regression analyses were performed in turn, with recovery rating (recovered v. partial/not recovered) by interviewer, child and mother used in turn as three dependent variables. The social data used as independent (predictor) variables and entered into the analyses as dichotomous factors were: undesirable life events (none/one or more), friendships (good or moderate/poor), recent social achievements (none/one or more), maternal confiding relations (good/moderator or poor) and maternal distress (absent/present). The duration of follow-up was also included with the social data subsequent to disorder. The influence of age, sex and pubertal status on the associations between social data and recovery was examined in all analyses.

Two categories of social information were used as independent (predictor) variables:

(a) social data from before onset of disorder
(b) social data after onset of disorder.

(a) The 21 predominantly anxious cases and the 28 predominantly depressive cases were cross-tabulated independently with each of the five social factors measured *before* the onset of disorder, but there were no significant relationships with poor recovery. For example, according to whose ratings of recovery are used, 55–75% of recovered cases (anxious or depressed) experienced one or more undesirable life events before onset compared with 33–75% of non-recovered cases; 40–60% recovered and non-recovered cases experienced no social achievements. The other three social factors were also reported in equivalent proportions by recovered and non-recovered cases. When logistic regressions were carried out for social factors before onset, none of the factors were significantly associated with recovery in any of the three analyses. Thus, social and family adversities or achievements occurring in the 12 months before the onset of either anxious or depressive disorders do not appear to influence the course of disorder.

(b) Table 3 shows the 21 predominantly anxious and 28 predominantly depressed cases rated as recovered or partially/not recovered on the three measures of recovery cross-tabulated with each of seven social factors (life events being further specified to form three separate factors) in the 12 months *after* onset of disorder. There was no significant relationship between poor recovery and any of the factors. Three logistic regression analyses were then carried out using the seven social factors as independent predictors together with diagnosis and duration of follow-up. In all three logistic regressions, the dependence of recovery on diagnosis, events (undesirable), achievements (none), maternal confiding relations (poor), maternal distress (present), friendships (moderate/poor) and duration of follow-up, showed that these variables failed to influence recovery except for:

Table 3
The life experiences of anxious ($n = 21$) and depressive ($n = 28$) cases rated as recovered or partially/not recovered by child, mother or psychiatrist in the period of time between onset and follow-up

	Recovery according to:											
	Child				Mother				Psychiatrist			
	Anxiety		Depression		Anxiety		Depression		Anxiety		Depression	
	yes ($n = 18$)	no ($n = 3$)	yes ($n = 12$)	no ($n = 16$)	yes ($n = 13$)	no ($n = 8$)	yes ($n = 15$)	no ($n = 13$)	yes ($n = 9$)	no ($n = 12$)	yes ($n = 14$)	no ($n = 14$)
One or more undesirable independent life events	7 (39%)	0 (0%)	2 (17%)	4 (25%)	4 (31%)	3 (38%)	3 (20%)	3 (23%)	1 (11%)	6 (50%)	3 (21%)	3 (21%)
One or more undesirable dependent events	5 (28%)	1 (33%)	4 (33%)	5 (31%)	4 (31%)	2 (25%)	3 (20%)	6 (46%)	2 (22%)	4 (33%)	4 (29%)	5 (36%)
Desirable events	5 (28%)	1 (33%)	6 (50%)	11 (69%)	3 (23%)	3 (38%)	7 (47%)	10 (77%)	2 (22%)	4 (33%)	7 (50%)	10 (71%)
No social achievements	7 (39%)	1 (33%)	4 (33%)	7 (44%)	5 (38%)	3 (38%)	4 (27%)	7 (54%)	5 (55%)	3 (25%)	5 (36%)	6 (43%)
Poor maternal confiding relations	3 (17%)	0 (0%)	2 (17%)	7 (44%)	2 (15%)	1 (12%)	2 (13%)	7 (54%)	2 (22%)	1 (8%)	3 (21%)	6 (43%)
Moderate/poor friendships	0 (0%)	0 (0%)	1 (8%)	7 (44%)	0 (0%)	0 (0%)	0 (0%)	8 (61%)	0 (0%)	0 (0%)	1 (7%)	7 (50%)
Maternal distress	9 (50%)	1 (33%)	3 (25%)	5 (31%)	7 (54%)	3 (38%)	4 (27%)	4 (31%)	5 (55%)	5 (55%)	3 (21%)	5 (36%)

(a) recovery as judged by child – diagnosis *and* friendships (deviance 14.66, d.f. 2); diagnosis, allowing for friendships (deviance 4.82, d.f. 1); friendships, allowing for diagnosis (deviance (4.69, d.f. 1)
(b) recovery as judged by interviewer – duration since discharge *and* friendships (deviance 14.10, d.f. 2); friendships, allowing for duration (deviance 4.96, d.f. 1); duration, allowing for friendships (deviance 9.00, d.f. 1)
(c) recovery as judged by mother – friendships (deviance 15.70, d.f. 1).

In psychological terms the results suggest that moderate/poor friendships subsequent to the onset of depression is the only factor reported by all respondents which exerts a negative influence on outcome. It could be argued that children who are not recovered may over-report undesirable experiences and difficulties including with friendships, in their lives. However, since all three respondents' logistic regressions are in the same direction the statistical interaction between moderate/poor friendships and diagnosis may reflect a valid psychological appraisal of the child's friendships since the onset of their depressive disorder. In addition, the analysis suggests that interviewers are influenced in their judgements of the degree of recovery by the duration of disorder.

Table 4 cross-tabulates recovery with diagnosis and the quality of friendships. These findings show that moderate to poor friendships are reported in 88% (children and interviewers) and 100% (mothers) of cases diagnosed as depressed at presentation and rated as not recovered at follow-up. By contrast, anxious children rated as not recovered at follow-up are reported as having relatively good friendships by mothers, children and interviewers.

Table 4
The proportion of children with good or moderate/poor friendships diagnosed as anxious or depressed at the time of presentation of disorder and rated as recovered or not recovered at the time of follow-up

	Diagnosis at presentation			
	Anxious (*n* = 21)		Depressed (*n* = 28)	
	poor/ moderate friendships	good friendships	poor/ moderate friendships	good friendships
Children's report[1]				
recovered	0	18 (86%)	1 (12%)	11 (55%)
not recovered	0	3 (14%)	7 (88%)	9 (45%)
Mother's report[2]				
recovered	0	13 (62%)	0	15 (75%)
not recovered	0	8 (38%)	8 (100%)	5 (25%)
Psychiatrist's report[2]				
recovered	0	9 (43%)	1 (12%)	13 (65%)
not recovered	0	12 (57%)	7 (88%)	7 (35%)

1. $\log[p(\text{recovery})/p(\text{no recovery})] = -0.3549 + 2.147\ \text{friends}^{*} + (-1.591)\ \text{diagnosis}^{**}$
standard error = (1.315) (1 159) (0.7655)
[*scaled deviance = 4.69, d f. 1; **scaled deviance = 4 82, d.f. 1]
2. $\log[p(\text{recovery})/p(\text{no recovery})] = -10.18 + 10.66\ \text{friends}^{*} + 0.6131\ \text{diagnosis}^{**}$
standard error = (25.63) (25.62) (0.6846)
[*scaled deviance = 16.18, d.f. 1; **scaled deviance = 0 82, d.f. 1]
3. $\log[p(\text{recovery})/p(\text{no recovery})] = -2\ 853 + 2.585\ \text{friends}^{*} + 0.9087\ \text{diagnosis}^{**}$
standard error = (1.247) (1.167) (0.6425)
[*scaled deviance = 6.89, d.f. 1; **scaled deviance = 2 04, d.f. 1]

Numbers in the equations are estimates with standard error in parentheses. Scaled deviance approximates χ^2 if term in model is zero. In each case we are looking at the significance of one of the two factors (friendships and diagnosis) allowing for the possible effect of the other.

The entry of age, sex or pubertal status into the equation did not influence the findings. In psychological terms this suggests that depressed but not anxious children may be at risk from moderate/poor friendships subsequent to the onset of disorder (between 7 and 16) or stage of development, independent of sex. The sample numbers in all three regressions are too small to determine the type of interaction between depression and moderate/poor friendships.

Discussion

These findings confirm other recent reports that the outcome of depression in school-age children and adolescents is poor, with up to 50% of the children reported as having persistent or relapsing symptoms. The findings indicate that the course of some anxiety disorders may also be worse than previously thought. Anxious and depressive disorders may be independent in some cases and represent different forms of emotional disorder. Further research should be carried out however to delineate the comorbidity and evolutionary relationship of anxious and depressive emotional disorders at onset, during their course, and at outcome.

The study demonstrates that adults and children do not wholly converge in their perception of childhood well-being. For example, interviewers may rate greater improvement in cases further from discharge (the time of which they are often given by the family). Parents may not be as aware of internal emotional and cognitive symptoms in their children as they are of observable changes in their behaviour. Children and adolescents are capable of reporting their internal symptoms but may (a) be overoptimistic about their well-being, (b) underestimate or fail to comprehend mental symptoms, or (c) provide socially desirable answers. Children may, to a large extent, provide reliable and valid information about their own mental state, but skilled interviewers as well as comprehensive and systematic interviews are required. Such interviews may be insufficient on their own, particularly in younger school-age children.

No significant alterations were found for three factors (friendships, maternal distress and recent achievements) occurring before onset and between onset and follow-up. Improvements were reported in maternal confiding relations and fewer children were exposed to recent undesirable life events, but these improvements did not significantly influence the recovery ratings. No type of desirable or undesirable life event or maternal adversity, before or after onset, exerted an effect on recovery. In this study the onset of disorder did not result in children becoming increasingly prone to life events.

These findings suggest that improving parent well-being, minimising exposure to undesirable events or promoting circumscribed social achievements may be insufficient to alleviate psychopathology in the child. Perhaps maternal and family reports of improvements should not be used as the sole clinical criterion for judging the child's improvement. Mothers (and fathers or other adult carers) whose own social relations have improved may reappraise their child's mental state favourably even if the nature of symptoms has remained much the same.

Despite differences in recovery ratings between child, mother, and interviewer, all report that moderate to poor friendships *after* onset was associated with poor recovery. This appears more likely for children rated as depressed at follow-up. We have previously reported that friendship difficulties before onset of disorder do not predict the type of diagnosis (Goodyer *et al*, 1989). There may therefore be a specific association between the onset of depression and the maintenance (or worsening) of subsequent poor friendships in this age group. These results may have one of two causes. Firstly, this effect may be 'social and direct', that is, the social behaviour of depressed children has a negative effect on the social behaviour of their friends. Secondly, this effect may be 'cognitive and indirect', that is, the negative thinking state of depression (which is absent in anxiety) reduces prosocial behaviour necessary for friendship development or maintenance, such as co-operation and intimacy as well as decreasing periods of necessary conflict. Clinical interviews should resolve whether social difficulties are due to abnormal beliefs or cognitive distortions in the child, or altered behaviour such as social withdrawal perhaps as a consequence of other symptoms (e.g. loss of energy or interest).

The findings in this paper must be taken conservatively, as a number of problems are apparent. Firstly, it could be argued that children's reports of friendship difficulties were confounded by the presence of depressive cognitions resulting in an over-reporting of friendship deficits. In this study, confounding of measures may have occurred as social data and recovery information were collected by the same researcher (we believe confounding was substantially minimised through the employment of contextual ratings; moreover, the findings are predominantly negative).

Secondly, our sample is small and derived from a clinic with tertiary referral responsibilities. Our results may not reflect the recovery of affective disorders in the general population. The findings do, however, appear to support previous research from both clinic and community studies conducted abroad on the short-term recovery of these disorders.

Thirdly, our interview method was not sensitive enough to determine episodes of illness and periods of normal mental functioning during follow-up. We cannot tell, therefore, whether poor recovery is related to persistent or episodic disorder for either diagnosis.

Fourthly, the sensitivity of our diagnostic categories could be improved through the use of more comprehensive and systematic interview procedures.

Fifthly, poor recovery may be a consequence of factors not measured in this study but related to socialisation. Adverse temperamental factors in the child may increase the risk for both depression and friendship difficulties (Buss & Plomin, 1984). Little is known of the role of temperament in the onset or course of anxious and depressive disorders in this age group and the matter warrants further study (Graham & Stevenson, 1987; Boudreault & Thivierge, 1987).

Sixthly, we may have been insensitive in our measures of family relationships. For example Puig-Antich *et al* (1985) suggested that deficits in verbal affective communication with parents and siblings were significantly more likely in pre-pubertal depressive cases than anxious cases or controls.

Finally, we were not able to investigate the potential effects of treatment on the outcome of disorder or the likelihood of experiencing desirable or undesirable social experiences. Anecdotally, the case-note information suggested that one in three of the families of depressed children may have terminated treatment against medical advice compared with one in five of the families of anxious children. The case-note information available to us was insufficient for systematic use in this study. The processes involved in treatment compliance and effectiveness clearly warrant investigation in future longitudinal studies on the outcome of emotional disorders in this age group.

The general outcome of childhood emotional disorders seen in clinic settings may be less favourable than previously considered. Recent maternal adversities and undesirable life events that are potentially causal factors in the onset of these disorders appear to exert no influence on their outcome. Improvements in such social adversities that are present at the time of referral may be necessary but insufficient for improvements in child psychopathology. In addition maternal adversities and life events (both undesirable and desirable) that occur after diagnosis do not appear to influence the general outcome of anxious or depressive disorder. The onset of a depressive illness at school age may adversely influence the course of social cognitive development through effects on friendships.

Appendix

Criteria for emotional disorder

The subjects were identified as suffering from emotional disorder as follows:

(a) Mothers (or their surrogates) completed the Rutter A(2) parent questionnaire on their first visit to the clinic. Those children who were definitely conduct-disordered on the basis of their scores were excluded. Those cases who were definitely emotional or mixed disorders and those whose scores were ambiguous (i.e. too low and therefore uninterpretable) were subject to a clinical screen.

(b) The clinical screen consisted of mental state examination of the child and interview with the mother, in all cases, and family interviews in a substantial proportion (approximately 50%).

Following these routine procedures one of the authors (IG) established with the clinicians if the child was suffering from an emotional disorder according to the following criteria:

> at least two-week duration, with predominant features of altered mood characterised by:
> anxiety, fearfulness, sadness or misery, accompanied by one or more of the following features: phobic or obsessional symptoms, sleep disturbance, eating disturbance, alimentary symptoms, social withdrawal (including school refusal).

Cases whose clinical picture contained these features but were dominated by behavioural characteristics such as lying, stealing, firesetting or destructiveness were excluded. Where clinicians remained in doubt ($n = 10$) children were re-interviewed by IG and a consensus diagnosis agreed. Of these ten cases four were included in the study. Finally, all cases were subject to two further classifications:

(a) Anxiety-dominant disorders present with marked features of fearfulness, phobias, obsessions and somatic symptoms (headache, abdominal pain and other non-specific pains). Features of misery and sadness were transient or absent.

(b) Depressive-dominant disorders present with marked and persistent features of misery and sadness accompanied by one or more negative thoughts (hopelessness, helplessness, suicidal ideation, poverty of thought); and one or more somatic features (undesirable alteration in sleep, appetite, energy, performance). Anxiety symptoms may also be present but are not predominant clinical features. Therefore, no concurrent diagnosis of anxiety was made.

Life events

The Revised Newcastle Child and Family Life Events Interview was used (Goodyer *et al*, 1985, 1988). The schedule was administered to the mothers of all the subjects. Two ratings of life events were made by the researchers:

(a) the likelihood that a life event was independent of illness

(b) the degree to which an event would exert an undesirable effect on the child likely to last days or weeks.

In addition, events likely to be considered desirable were recorded. Desirable events were not subject to qualitative ratings but excluded social achievements of the child which were collected separately. Both interviewers were trained in methods of rating. A random sample of interviews ($n = 15$; no. of events $= 50$) were rated by the main author on the two five-point scales for degree of undesirability and independence for each event respectively. The percentage concordance between interviewers and IG ratings was 80% exactly and 90% to within one point of each scale for all events.

Only events rated moderately to severely undesirable were included in the analyses. For the present study both independent and dependent events were included in the analysis. We reasoned that: (a) events independent of any continuing disorder, and undesirable, may exert further negative effects on well-being, and (b) emotional disorders may render a child prone to life events and thereby increase the likelihood of exposure to undesirable events through alterations to the environment as a consequence of psychopathology.

Recent social achievements

We defined social achievement as "any event that had social and personal connotations of desirability and would be seen by others (peers, teachers and relatives) as expressing a degree of personal competence" (Goodyer *et al*, 1990). Four areas of social achievement were considered.

(a) Education. This included recent examinations and educational achievements such as school project work.

(b) Physical achievements. These included participation in activities that resulted in any form of trophy, badge, award or recognition.

(c) Art/craft/technology achievements. These included completion of a course, awards, finishing a project or performing or exhibiting to an audience.

(d) Community achievements. These included taking part and completing organised activities in the community such as charity walks or voluntary work.

In areas b, c and d, successful completion was a necessary criteria for all achievements. Qualitative judgements of relative social success between children were not used. We judged 'success' according to the child's and parent's perceived expectations. Therefore all children were capable of some social achievement if they had participated successfully and received recognition for their efforts. The measure consisted of the number of social achievements in the time period since diagnosis.

Measurement of friendships

A semistructured interview schedule was used which had been developed to obtain substantive information about the availability, adequacy and intimacy of friendships at home, school and at play (Goodyer *et al*, 1989). The semistructured interview was conducted with both child and mother (or main carer) independently but at the same period. The description of the child's friendship behaviour used for rating consisted of the confluence of child and mother's contextual information. Clearly in some cases discrepancies may occur in reporting. Clarification and consensus between mother and child was obtained at the time of interview. Discrepancies were few (less than 10% of items asked) as we had found previously when recording the children's friendships before the onset of disorder (Goodyer *et al*, 1989).

Friendship was rated on a three-point scale: good, moderate or poor, based on descriptions from all information. We have previously reported that anxious and depressive disorders are significantly more common in those school-age children who report moderate to poor friendships in their own lives (Goodyer *et al*, 1989).

The rating of friendships was made by the researchers (EG & JG) following training with IG. We have previously reported satisfactory reliability between raters for this three-point measure (Goodyer *et al*, 1989).

The measurement of maternal confiding relationships

We measured mother's perceived support in terms of the availability, adequacy and intimacy of maternal confiding relationships based on the work of Brown & Harris (1978) and Henderson *et al* (1981). A semistructured interview was developed in which mothers were asked questions relating to the frequency, contact, duration and setting of time spent together. The researchers used all information to rate the quality of maternal confiding relations as good, moderate or poor. We have previously shown that anxious and depressive disorders in school-age children are significantly more common when mothers report poor maternal confiding relationships in their own lives (Goodyer *et al*, 1988).

The interview placed emphasis on establishing the long-term quality of maternal confiding relationships subsequent to diagnosis. We did not specifically measure marital relations as we believed that a number of mothers would receive support outside the marriage, and a proportion of these women would be single (20% had been single at the time of entry into the original study). We have previously shown satisfactory test–retest reliability ($k=0.8$) for mothers' responses to the items in the schedule (Goodyer *et al*, 1988). In addition, we have shown that two pairs of raters show good agreement (80%) for rating the quality of confiding (Goodyer *et al*, 1988). Finally, we have also shown that for this group of mothers the quality of confiding relationships was not influenced by past maternal psychiatric history, being a single parent, having had a personal relationship for less than 12 months at the time of interview, having three or more children (Goodyer *et al*, 1988).

The presence of maternal distress

Mothers completed the Rutter Malaise questionnaire (Rutter *et al*, 1970). This questionnaire has been shown to be a reliable indicator of maternal distress and associated with social adversity (McGee *et al*, 1985). Mothers who scored seven or more were considered distressed. We have previously shown that the presence of maternal distress does not result in retrospective over-reporting of life events (Goodyer *et al*, 1988).

Finally, we have shown that there were no social class biases in the social data collected in the original study. This suggests that social class does not appear to significantly influence the reporting and measurement of the dependent variables used (Goodyer *et al*, 1988, 1989).

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Care of Chronic Neurotic Out-patients by Community Psychiatric Nurses
A Long-Term Follow-Up Study

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Ninety-nine neurotic patients from a controlled trial of CPN v. psychiatric out-patient aftercare were followed up seven years later. Of the 92 survivors, 76 were successfully interviewed. Few differences were found between the groups. Chronic mild symptoms and moderate social disability persisted, and tended to worsen a little. Treatment patterns persisted for one to two years beyond the original study; the CPN group had more CPN contacts, fewer psychiatric out-patient contacts and less psychiatric care. Thereafter, more out-patients were discharged from psychiatric care and care patterns for the two groups became similar. Out-patients attended more non-psychiatric out-patient clinics than the CPN group, but it is possible that this reflected pre-existing differences. About a third of patients remained in contact with the psychiatric service during follow-up.

Community psychiatric nursing appeared in Britain in the mid-1950s at Warlingham Park Hospital, Surrey, and Moorhaven Hospital, Devon. Its development paralleled the falling bed occupancy and emphasis on short-term admission and community care which found their expression in the Mental Health Act 1959. Since the early 1970s there has been a dramatic increase in the number and availability of community psychiatric nurses (CPNs). The historical development of the service was documented by Hunter (1974) and reviewed by Carr (1979) and Griffith & Mangen (1980).

Undoubtedly, the availability of phenothiazines stimulated much of the growth of community nursing and provided an important focus in its function. By the second half of the 1970s the role of CPNs in the long-term care of schizophrenics (the largest group of CPN patients in Parnell's (1977) survey) was well established although not extensively researched (Pasamanick *et al*, 1964; Warren, 1971; Robinson, 1972; Hunter, 1978). Parnell's survey showed a varied pattern of organisation, encompassing supervision of medication, support, psychotherapy and family intervention. The expansion of out-patient care which had led to a major increase in the proportion of neurotic patients was reflected in CPNs' case loads. In Parnell's study, depression was the second most common diagnosis in CPN patients. Recent work from Salford (Wooff *et al*, 1986) has confirmed this continued involvement and has voiced concern about the CPNs' role with this patient group when operating from a primary-care base.

A controlled evaluation of CPN intervention in the care of such patients was carried out between 1977 and 1980 in this department (Paykel *et al*, 1982; Mangen *et al*, 1983; Paykel & Griffiths, 1983). Unlike the CPNs studied by Wooff *et al*, these nurses all worked within a specialist mental health team and their patients had all received treatment by the psychiatric team. Chronic neurotic patients were allocated on discharge from in-patient or day-patient care (34%) or after a minimum of 18 months' attendance at the out-patient (OP) clinics (66%). Patients were accepted for the study if their treating team considered they required at least another six months of OP care. A total of 99 patients completed the treatment requirement. Such a treatment plan was possible with standard catchment-area teams. Although no differences were demonstrated in symptom levels, social adjustment or family burden, over time CPNs achieved greater consumer satisfaction. Contact frequency was initially higher than in OP care but this diminished. Contact with psychiatrists was markedly diminished and there was an increased rate of discharge from psychiatric care in the CPN group by the end of 18 months.

Despite low levels of symptoms and social handicap, chronic neurotic patients impose a considerable burden on psychiatric services because of the long-term nature of their care. The paucity of information on their natural history or on the impact of long-term care on their outcome, requires us to look closely at the increased rate of discharge to primary care in the CPN group.

Patients were therefore followed up nearly eight years after their intake into the original study to obtain answers to three main research questions.

(a) What is the overall outcome of these disorders? Are the patients still symptomatic and dysfunctional after so many years?
(b) What is the long-term efficacy of CPN care of chronic neurotic patients compared with standard OP care in terms of symptoms and social adjustment?
(c) What are the actual patterns of treatment received in the long term by patients in these two groups? Does the trend towards more discharges in the CPN group continue?

Because of the long, retrospective time periods, a cost analysis (as conducted in the original study) was not feasible.

Method

The sample comprised 99 subjects from the original study who completed the qualifying six months of treatment in that study design. Only 71 of these subjects were followed up for 18 months and reported in detail in the original papers. Drop-outs between 6 and 18 months were due to poor co-operation and moving away, with some planned study terminations at 12 months to permit timely completion of the research. Separate analysis on the full 99 indicated no differences from the 71. It was decided to interview all patients who could be traced, lived in the UK and whose family doctor agreed to their being approached.

Follow-up assessments were conducted between six and eight years (mean 7.06 years) after termination of the original study. Year one of follow-up is defined as starting 18 months after intake and is applicable to all patients. Not all the patients in the original study completed the full 18 months: seven completed 12 months and two six months, and the former therefore have gaps of six months and the latter 12 months between termination and the start of the follow-up data. Neither the data from these gaps nor the data available for an eighth follow-up year in five patients are individually presented or included in the calculated totals.

Assessment was conducted by the research psychologist (AE) in a single interview lasting between one and two hours, in the patient's home. A modification of the original social history was repeated to ascertain any changed demographic and social characteristics along with relevant administrative data.

The Clinical Interview for Depression (Paykel, 1985), modified slightly as in the original study, was repeated. This semistructured interview contained 28 items to cover depressive and neurotic symptoms rated on seven-point scales with defined anchor points. It was supplemented by global ratings for severity and the Raskin three-area scale for depression (Raskin *et al*, 1976) with a parallel scale for anxiety. All individual ratings are for the preceding month and the global rating for the last six months.

The Social Adjustment Scale (SAS; Weissman & Paykel, 1974) is a 45-item semistructured interview covering five main areas:

(a) work (as housewife, worker or student)
(b) social and leisure
(c) extended family
(d) marital
(e) parental.

It measures behaviour, feelings and personal satisfaction. Individual items are on five-point and globals on seven-point scales, all with well identified anchor points. All ratings refer to the preceding two months. As with the clinical interview, higher scores indicate greater disturbance.

A longitudinal treatment record was completed for each individual year of follow-up for each patient. This recorded information on the use of psychiatric and general OP clinics, day-patient and in-patient services, psychotherapy, contact with general practitioners, psychologists, social workers and voluntary agencies. Local psychiatric notes were used to obtain a final accurate set of information. General hospital notes were not examined nor, because of their low yield in the original study, were general practitioners' notes or social service records.

Results

The follow-up was relatively complete and all but three of the 99 subjects were traced. Seven subjects had died. Of the remaining 13 who were not followed up, two were too ill, two were abroad, eight refused and one did not complete the interview. Among the survivors 76 (83%) were fully interviewed (37 CPN, 39 OP).

The initial characteristics of the 76 patients interviewed are displayed in Table 1. There are no significant differences between the original 99 subjects and the 76 followed up nor beween the CPN and OP groups. Subjects lost to

Table 1
Initial characteristics of the follow-up patients

	OP ($n=39$)	CPN ($n=37$)
Demographic		
Mean age: years	44.8	42.8
Male	14	6
Female	25	31
Single	4	3
Married	23	24
Separated/divorced/widowed	11	10
Original primary diagnosis		
Depressive neurosis	14	14
Anxiety or phobic neurosis	13	13
Other neurosis	4	2
Depressive psychosis	3	4
Personality disorder	5	4
History of study intake		
Recent out-patient	26	26
Recent in-patient/day patient	13	11
Months of present illness (mean)	33.3	30.8
Months of recent continuous treatment	22.7	27.7

No significant differences found at the $P<0.05$ level using χ^2 and t-test.

follow-up were shown to be significantly older than those interviewed (49.6 years v. 43.8 years, $P<0.05$ by t-test). There were no other significant differences.

Table 2 displays a summary of the major symptom and social adjustment data for the follow-up patients at original intake, original study termination and follow-up. Symptom levels were generally mild. Mean score on the clinical interview (sum of the individual items divided by their number) returned on follow-up to intake level. The three-area anxiety score and three-area depression score, rated in the same interview, showed the same pattern. Only on the global severity rating do treatment gains appear to be maintained and this is a more impressionistic measure than the others. On all four symptom measures the CPN group scored marginally less at each assessment, although this never reached significance. When change scores were calculated the two groups were closely comparable.

The mean SAS scores are also presented in Table 2. Means are based only on patients who could be assessed in the appropriate area on all three occasions. At follow-up, 26 patients had retired while none had in the original study. There were, therefore, 'work/housewife' role scores available on only 50 patients. Only 48 patients still had a marital relationship to assess and 36 a parental relationship to living-in children. The data for these restricted samples did not show any significant differences between the two treatment groups.

Social dysfunction levels were low apart from social and leisure activities where pathology (mainly representing diminished social interaction) was noticeably increased from the initial assessment in both treatment groups. There were no significant differences between the groups in social adjustment. The number of patients in paid employment

Table 2
Major symptom score and social adjustment means at each rating period

	OP ($n=39$)	CPN ($n=37$)	t-test
Clinical interview			
initial	1.93	1.80	1.16
termination	1.57	1.48	1.13
follow-up	1.93	1.84	0.58
Global severity of illness			
initial	3.15	3.03	0.72
termination	2.50	2.31	0.85
follow-up	2.36	2.30	0.25
SAS social and leisure			
initial	2.10	2.17	0.43
termination	1.95	1.93	0.12
follow-up	2.47	2.55	0.41
SAS extended family			
initial	1.63	1.67	0.28
termination	1.35	1.49	1.50
follow-up	1.55	1.71	1.35
SAS global adjustment (global 1–7 range)			
initial	2.97	2.68	1.22
termination	2.57	2.48	0.29
follow-up	2.54	2.96	0.90

Table 3
Numbers of different types of contacts during each year of follow-up

Year	OP No. of subjects in contact per year	CPN No. of subjects in contact per year	χ^2
CPN contacts			
1	1	10	7.03*
2	1	7	3.63
3	0	4	2.46
4	0	2	0.54
5	0	3	1.44
6	0	0	–
7	1	3	0.21
Total	2	14	9.91*
Total contacts			Mann-Whitney U-test,
median	0	0	$Z=-3.3838$**
mean (range)	0.56 (2–20)	7.47 (1–136)	
Psychiatric contacts			
1	20	12	2.32
2	16	10	1.26
3	11	10	0
4	12	10	0.03
5	9	9	0
6	9	8	0
7	9	8	0.02
Total	20	19	0.07
Total contacts			Mann-Whitney U-test,
median	2.5	1.5	$Z=-0.3321$
mean (range)	12.67 (1–20)	11.95 (1–13)	
Team contacts			
1	24	18	1.04
2	17	15	0.08
3	12	12	0.00
4	12	11	0.03
5	11	12	0.00
6	10	9	0.02
7	10	10	0.00
Total	27	25	0.03
Total contacts			Mann-Whitney U-test,
median	6	4	$Z=-0.0211$
mean (range)	17.87 (1–84)	23.74 (1–171)	
Non-psychiatric out-patient attendances			
1	13	3	6.10*
2	13	3	6.10*
3	14	7	2.15
4	16	10	1.26
5	17	9	2.58
6	17	9	2.58
7	10	14	0.34
Total	29	23	1.11
Total contacts			Mann-Whitney U-test,
median	8	2	$Z=-2.8169$
mean (range)	18.7 (1–191)	4.6 (1–47)	

*$P=<0.01$, **$P=<0.001$.

decreased by 15 (five retired, 10 unemployed). Only four patients took up paid employment during the seven years of follow-up as opposed to 15 during the 18 months of the original study. Their increasing age and the changed economic climate are, of course, relevant.

Table 3 summarises the CPN contact over follow-up. The number of subjects in contact with the service each year is shown, and the mean and median number of contacts over the whole seven years. There was negligible use of the CPN service by the OP group, with only one patient in contact for the first two years of follow-up and one referred in the seventh year. Contact by the CPN group showed a steady decline and, apart from the three new patients in year seven, included no new episodes of contact. While the total usage of CPN contact was significantly greater in the CPN group for the whole follow-up period (a mean of 7.47 contacts v. 0.56), this was predominantly early in follow-up.

A major contact during follow-up for both groups was the psychiatrist. A total of 20 in the OP group and 19 in the CPN group contacted a psychiatrist during follow-up, with mean frequencies of 12.67 and 11.95 (Table 3). There were no significant differences in either the number in contact or the frequency of contact between the two groups.

While total psychiatrist contact frequency is very similar for both groups, the OP group had higher numbers in contact with consultants over follow-up than the CPN group (15 v. 10) with a higher total contact frequency (9.41 v. 2.55 per year). While the overall figures are not significant, the OP group contact frequencies with consultants are significantly higher ($P<0.05$, by Mann–Whitney U-test) in years one, two and seven. A reverse pattern was found for contact with the junior psychiatrist with 13 in contact with the OP group against 17 in the CPN group, but this difference is not significant.

Total contacts with the psychiatric team over follow-up are also shown in Table 3. There were no significant differences between the two groups. The trend towards more discharges in the CPN group was maintained in years one and two of follow-up. The drop in the number of subjects in the OP group in contact in year three suggests that discharge was merely delayed in this modality group.

This overall measure of contact was examined in greater detail. In-patient and day-patient care were rarely used and showed no difference between the two groups. Seven CPN patients were responsible for a total of 18 episodes of care during follow-up and six out-patients for 13 episodes. The OP group's admissions were concentrated in the earlier part of follow-up. The CPN group overall had a mean duration of admission of 3.7 weeks v. 5.46 weeks in the OP group.

Most non-psychiatric contact was with the patient's general practitioner. Only one patient in each group had no contact with a general practitioner during the seven years of follow-up. The lowest number in contact in any year was 29 in the CPN group and 30 in the OP group. Mean total contacts for the two groups were 39.6 for the CPN and 40.3 for the OP group, averaging out at about one visit every two months. Casualty attendances were also examined but found to be minimal – eight CPN patients and six out-patients attended accident and emergency departments on a total of 16 occasions over seven years.

There was a significantly higher use of non-psychiatric out-patient clinics by the OP group, with a mean of 18.7 visits over the seven years compared with a mean of 4.6 for the CPN group. Apart from year seven, the number of patients attending from the OP group always exceeded that from the CPN group, significantly so in years one and two.

Identifying new episodes of referral to out-patient departments is not possible with any great confidence. Transition from a year with no contact to a contact year and then back to a non-contact year was taken to indicate an episode of out-patient care. By this measure the OP group had slightly more episodes (34 v. 31) and their episodes were on average longer (2.94 years v. 1.74 years). Neither difference was statistically significant.

Discussion

At follow-up, this group of chronic neurotic out-patients shows essentially the same level of symptom scores and social dysfunction as at intake. This close similarity on all symptom measures other than the more impressionistic global severity of illness requires consideration. After seven years, this group is apparently complaining of the same levels of depression, anxiety, and general distress as when they first entered the treatment study. Treatment appears to have successfully reduced distress during the period of contact, but not to have endured for seven years. There is no suggestion of the natural waning of symptoms over time more characteristic of discrete illness episodes. These findings must be interpreted with caution. Patients were usually entered into the original study after the acute episode had remitted, symptom levels were low and changes modest.

There are two possible interpretations. Firstly, the research interview may be measuring an enduring 'mental set' – a chronic, fairly stable, level of distress and dissatisfaction which was temporarily ameliorated by active treatment – OP or CPN. This treatment effect might be a measure of the social importance of this contact for otherwise isolated individuals. Clinical and social functioning as well as consumer satisfaction, however, continued to improve towards the end of the original study despite falling 'raw' contact rates (especially in the CPN group). It is unlikely, therefore, that any such effect is purely supportive but probably works through improving the patient's sense of self-esteem and personal effectiveness. It is open to speculation how long this period of comparative reduction in distress persisted and whether it differed for the two groups.

A second interpretation of these findings is that the identical symptom measures at follow-up may represent a delay in an otherwise slow clinical deterioration. The social functioning of these patients showed a small overall deterioration – particularly in social isolation. There was a gradual erosion of their social networks with retirement, children leaving home and spouses dying. All of this might contribute to clinical deterioration. Such an interpretation would require careful evaluation and deserves serious consideration. In other areas of psychiatry (most notably recently in the OP care of chronic schizophrenics) the delaying or arresting of clinical and social deterioration has become the focus of intense clinical and research activity.

It is unlikely that any such long-term processes would be identified and effectively countered in an OP service staffed by psychiatrists on rotation. CPNs, however, can plan long-term, low-intensity psychosocial interventions. Present CPNs, unlike those in the original study, are now often experienced in the care of this patient group and have formalised training in the relevant individual and family techniques.

The original study, which randomly allocated chronic neurotic out-patients to either CPN or routine OP care, showed no differences in clinical or social functioning (Paykel *et al*, 1982). The CPN service achieved much greater consumer satisfaction and resulted in more discharges at 18 months. While these results were modest they did consistently favour the CPN-treated group and were becoming more pronounced towards the end of the study.

The absence of any differences between the two treatment groups in symptom levels at follow-up is hardly surprising. Original levels were generally low and no difference had been shown even during the active phase in the original study. What the impact would be of randomising the patients at referral rather than after discharge from in-patient or day-patient care or 18-months' OP care remains to be tested.

The ease with which a substantial population of chronic neurotic patients was obtained for the original study from general psychiatric out-patients highlights the considerable resource implications of this group. Reduction of contact without loss of efficacy is a worthwhile therapeutic target. We found a reduction in contact with psychiatric services over the follow-up period, but it is neither rapid nor complete. At termination of the original study 60% were still in contact with psychiatric services and this had only fallen to 42% after two years of follow-up and was still 25% at 7 years.

The increased number of discharges in the CPN group at the end of the original study represent planned-for and negotiated discharges with no evidence of rejection by patients or rapid re-referral. This advantage was maintained for the first year of follow-up. The OP group caught up in the second year, after which there was no difference. CPN care, with its advantages of continuity and planned targets (Paykel *et al*, 1982; Paykel & Griffith, 1983), had the effect of expediting discharge which was delayed in the OP group. These savings are more noteworthy given the imposed transfer to CPN care and also that, even including the early intensive contact phase, it was cheaper than routine OP care.

The rapid tailing off of CPN contact and low rate of re-referral to CPNs in follow-up contrasts sharply with the rapid increase in non-schizophrenic patients on CPN case loads during this period, reported in Salford (Wooff *et al*, 1986). CPNs in this study took their referrals from the psychiatric team, whereas in Salford they were attached to primary-care teams. Psychiatrists remained responsible for over half of the total contacts in these patients over the follow-up. Despite the results of the original study they continue to express concern that patients will feel rejected, or relapse, if transferred from OP care.

A very obvious difference in the two groups is their use of general medical and surgical out-patient facilities. Neither physical illness nor attendance at general medical and surgical out-patient departments had been controlled for in the original randomisation. As shown in Table 3, the number attending throughout follow-up was consistently higher for the OP group. The mean rate of attendance was also consistently higher in the OP group, virtually tenfold in the first two years (1.97 and 3.26 v. 0.18 and 0.45 respectively) and overall four times higher. It is possible, however, that there was an excess of seriously or chronically physically ill patients in the OP group. Figures from the original study do show greater contact with general medical out-patient departments in the OP group in the first six months (mean visits 1.33 v. 0.38, $P<0.05$). This significant excess contact is not found in the two succeeding six-month periods (0.84 v. 0.79 and 0.53 v. 0.43) or in the total 18 months (2.7 v. 1.6).

The high rate of neurotic disorders in medical out-patient departments is well documented (Shepherd *et al*, 1960). Powerful neurotic dependency needs may be just as potent in these clinics as in psychiatric out-patient departments. Similar aspects of this complex doctor/patient relationship may mitigate against successful discharge to primary care in both instances. As with psychiatric care, the optimal division between out-patient specialist responsibility and general practitioner responsibility in the management of long-term disorders is unclear and patient expectations may play an important part. It is possible that broader-focused, psychosocial interviews with the CPNs enabled their patients to distinguish better between dissatisfaction in their daily lives and 'illness' as such. As a result, the CPN group may have altered their expectations of, and relationship to, the medical profession.

One should not overlook the alternative interpretation that these increased general medical out-patient contacts represent greater success in identifying treatable physical illness. It could be argued that increased contact with the consultant psychiatrist in the OP group early on led to the identification of physical disorders which were referred to general out-patients.

The findings of this follow-up support the original study conclusions. CPN care appears to be as effective clinically and socially as standard OP care for chronic neurotic patients. Involvement of CPNs resulted in a modest increase in early discharge to primary care, and long-term follow-up showed no evidence of a reversal of this trend. The general picture over the first year of follow-up was of less use of psychiatric services in the CPN group, followed by a fall in the OP group to bring the two services level. Interpretation of the remarkable differences in general out-patient attendance is complicated because of an early suggestion of greater physical morbidity in the OP group. The unexpected nature of this finding underlines the need for CPN work to be carefully evaluated in detail to identify effective therapeutic activities. Assumptions about the specific skills and values of this emerging professional group cannot simply be translated from in-patient experience.

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Facial Dyskinesia: A 16-Year Follow-up Study

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The 109 female survivors of a mental hospital population surveyed in 1965 for facial dyskinesia were followed up 16 years later. The 99 survivors with non-organic brain syndromes were analysed. Prevalence of dyskinesia had risen from 18.4% to 46.5% during follow-up and its development was significantly associated with neuroleptic dosage. Enlarged ventricles on brain scans were significantly associated with dyskinesia, cognitive impairment and neuroleptic prescribing.

While a large number of prevalence studies on tardive dyskinesia have been published in the past three decades, follow-up studies have been few in number and limited in scope (Casey, 1985). Only recently have major prospective studies been initiated (Kane *et al*, 1982).

In 1965, a prevalence survey of facial dyskinesia was carried out at St Nicholas Hospital (Brandon *et al*, 1971). The original data provided a base for follow-up in 1981, 16 years later, which is reported here. One of the investigators (HAMcC) took part in both surveys. The findings on mortality have been reported elsewhere (McClelland *et al*, 1986).

This study examines:

(a) the dyskinesia status of the surviving female patients
(b) aetiological factors in the development of dyskinesia
(c) the association of cognitive impairment with dyskinesia, neuroleptic therapy and diagnosis.

Method

In the 1965 survey there were 910 patients (426 males and 484 females). The 1981 follow-up study was limited to the female patients. Of the original 484 females, 109 were traced and examined (77 in hospital and 32 in the community), 356 had died, 14 could not be traced, four had left the region and one refused to co-operate.

The 1965 survey records contained details of the patients' drug history and other physical treatments. The case notes were used for extraction of data during follow-up.

Details of medication were obtained at five-year intervals from 1965 onwards, with amounts being based on the prescribing for a 12-month period.

For neuroleptics, dosage tables were drawn up in terms of chlorpromazine equivalents (Davis, 1974) and the amounts graded as follows:

(a) small – 100 mg or less daily of chlorpromazine equivalent, or 12.5 mg of fluphenazine decanoate (or equivalent) every 3 weeks or less frequently
(b) moderate – between 100 mg and 400 mg chlorpromazine equivalent daily, or 25 mg fluphenazine decanoate (or equivalent) every 2–4 weeks
(c) large – amounts greater than in (b)
(d) for patients reaching 65 years of age or over, the definitions were set at 50% of the amounts defined above.

The neuroleptic items used were: (a) total neuroleptic amount prescribed during follow-up, (b) duration of neuroleptic treatment up to 1965, (c) duration of treatment up to 1981, (d) whether on neuroleptics at time of the 1981 examination, (e) whether free from neuroleptics in the period 1965–81, (f) change in pattern of neuroleptic amounts prescribed over the years (decreasing, stationary or increasing), (g) amount of neuroleptics prescribed in 1965.

For other drugs (benzodiazepines, antidepressants, anti-Parkinsonian and anti-epileptic agents), the specific items were: whether the patients were on these drugs in 1981, and whether the drugs were taken during 1965–81 (graded never taken, intermittently taken, continuously taken).

Details regarding neuropsychiatric illness, electroconvulsive treatment, insulin coma treatment and psychosurgery were obtained.

The 1965 survey assessed facial dyskinesia globally on a five-point scale (0 = nil, 1 = doubtful, 2 = mild, 3 = moderate, and 4 = severe). The follow-up examination in 1981 used the same scale. A simple Parkinsonian rating scale (as used in 1965) was also used, with items for loss of arm swing, plastic rigidity, cog-wheel rigidity, and tremor, to generate a four-point global item. Ratings were by consensus, with a minimum of two investigators being present at each examination. Examinations took 10–20 minutes, during which time the patient was involved in conversation and asked to perform simple manual tasks and exercises. Investigators tried to vary the arousal level of the patient. Whenever possible the patient was observed before and after the direct examination.

Two tests were used to assess intellectual impairment:

(a) the patient's subjective age against chronological age (Crow & Stevens, 1978)
(b) the Newcastle dementia scale (Blessed *et al*, 1968).

Table 1
Psychiatric diagnosis and dyskinesia status at follow-up

Diagnosis	Total number	No dyskinesia	Dyskinesia present			% dyskinesia present
			mild	moderate	severe	
Schizophrenia	62	35	15	10	2	43.5
Schizoaffective	15	7	5	3	0	53.3
Major affective	17	8	8	1	0	52.9
Other	10	8	1	1	0	20
Primary brain syndrome	5	4	1	0	0	20
Total	109	62	30	15	2	

Research diagnostic criteria in 1981 were based, as far as a case-record study would allow, on DSM-III (American Psychiatric Association, 1980) criteria. The diagnostic categories were 'schizophrenia', 'major affective disorders', 'schizoaffective disorder', 'other' (a non-organic heterogeneous group of paranoid psychoses, adjustment disorder, personality disorder) and 'primary organic' (dementia syndromes).

Computerised tomography (CT) was carried out on 27 patients in 1983/84 using an EMI 1010 scanner. The brain sections showing maximum ventricular size were selected and measured in triplicate using a Joyce Loebl Magiscan Image Analyser. The ventricular margins and the inner table of the skull were outlined manually using a light pen, and ventricular and brain areas measured by the Magiscanner (Reveley, 1985). The ventricle:brain ratio (VBR) was used in the analysis. The measurers were blind to psychiatric diagnosis and dyskinetic status. Both investigators measured all the CT scans and the correlation (*r*) between their measurements was 0.95. There was no evidence of any systematic difference between the raters.

Results

Table 1 gives details of psychiatric diagnoses (DSM-III criteria) in relation to dyskinesia status. The five patients with primary organic brain syndromes were excluded from subsequent analyses. Also excluded were five patients with a primary diagnosis of functional illness who had sustained a neurological complication (stroke, three; disseminated sclerosis, one; and no specific diagnosis, one).

Details of the dyskinesia status, according to age, of the 99 non-organic survivors are given in Table 2. The overall dyskinesia prevalence had risen from 18.4% in 1965 to 46.5% in 1981. The severity of dyskinesia also increased during follow-up. In 1965 there were six cases of moderate but no severe dyskinesia but by 1981 there were 14 moderate and two severe cases.

The 99 patients were divided into four groups.

(a) Dyskinesia positive in 1965 and negative in 1981. Of the six patients (mean age 67 years, s.d. 14), four had had moderate and two mild dyskinesia. Only three of the six had stopped neuroleptics by 1981.

(b) Dyskinesia positive in 1965 and 1981. Of the eight patients (mean age 76 years, s.d. 4), six had mild dyskinesia in 1965; three remained mild and three increased to moderate. Of the two with moderate dyskinesia in 1965 one remained unchanged and one improved to mild. No case with dyskinesia in 1965 had deteriorated to severe by 1981.

(c) Dyskinesia negative in 1965 and 1981. There were 48 patients (mean age 61 years, s.d. 12) in this group.

(d) Dyskinesia negative in 1965 and positive in 1981. There were 37 patients (mean age 69 years, s.d. 9), of whom 24 developed mild, 11 moderate and two severe dyskinesia. The two patients who developed severe dyskinesia were women in their late 70s who had commenced neuroleptics within the previous five years.

Eight patients had never received neuroleptics. All were dyskinesia-free in 1965, seven remained so in 1981, while one developed mild dyskinesia. A comparison was made with the 77 dyskinesia-free patients in 1965 who received neuroleptics, of whom 36 developed dyskinesia. Using Fisher's exact test the difference between the two groups does not quite reach significance ($P=0.06$, one-tailed).

Patients who converted from dyskinesia negative to positive by 1981 were compared with those who had remained negative throughout. Items analysed were neuroleptic items, other drugs, ECT, insulin coma, and psychosurgery. Depending on whether items could be graded as continuous or not, analyses were either by comparison of means allowing for covariates using the MANOVA procedure (SPSSX, 1988), or by postulating a logistic model for proportions (Everitt, 1977). Age, psychiatric diagnosis and the interaction of diagnosis with duration of illness were allowed for. *P* values quoted are one-sided.

Analyses of dyskinesia change were performed using three different groups: (a) mild cases of dyskinesia combined with moderate and severe cases, (b) mild cases withdrawn from the analysis, (c) mild cases grouped with the dyskinesia-negative cases. The *P* values quoted below are the results for these respective groupings, and are two-sided.

Neuroleptic prescribing. The items 'total duration on neuroleptics up to 1981' ($P=0.032$, 0.025, 0.034), 'increasing dosage of neuroleptics 1965–81' ($P=0.09$, 0.004, 0.004), and 'total amounts of neuroleptics 1965–81' ($P=0.001$, 0.002, 0.017) had varying levels of statistical significance.

Other treatment items. Only 'total amount of anti-Parkinsonian drugs' reached significant or near-significant levels ($P=0.032$, 0.023, 0.056).

Parkinsonism. The average Parkinsonism score in 1965 was higher in patients who later developed dyskinesia but, with allowance made for age, diagnosis, length of illness and interaction of length of illness with schizophrenia, the association was non-significant. If mild dyskinesia was combined with "no dyskinesia", or omitted from the analyses, there was a non-significant trend ($P = 0.07$).

Seventy-eight of the 85 patients in groups (c) and (d) were able to complete the Newcastle dementia scale and the subjective age test. The patients' subjective age responses were grouped by the difference to chronological age. The total dementia score ranged from nought to seven. Patients who refused to co-operate were not included. The patients who developed dyskinesia, compared with those who remained dyskinesia-free, scored (allowing for age) worse on cognitive tests, but at a non-significant level (dementia score $P = 0.081$; subjective age $P = 0.182$). P values given are one-sided as neurological abnormalities such as dyskinesia would not be associated with improved mental ability.

No significant association (in regression analyses) was found between neuroleptic items and poor cognitive ability as measured by dementia scores. Dementia scores significantly increased with length of schizophrenic illness ($P = 0.044$, two-sided) but not with the other diagnostic categories. In the regression analyses, age and interactions with length of illness and diagnosis were allowed for.

CT studies

In 1983 access was granted for brain scan studies. Twenty-seven patients gave full informed consent to this procedure. Four patients with a primary or secondary organic brain syndrome were excluded from analyses. Of the 23 left for study, 15 suffered from schizophrenia, three from major affective disorders, four from schizoaffective psychoses, and one from 'other' functional disorder. Nine of the 23 patients were 65 years or under (mean age 56.8 years (s.d. 6.2)) and 14 were over 65 years of age (mean age 77.4 years (s.d. 10.0)).

The over-65 age group had a mean VBR of 15.7 (s.d. 3.0) and the under-65 age group one of 9.78 (s.d. 2.1). The mean VBR for the different diagnostic groups, adjusted to the mean age, are: for the 15 patients with schizophrenia 12.85 (range 7.93–20.43); for the four with schizoaffective psychoses 13.90 (range 7.20–20.43); for the three with major affective disorders 12.90 (range 10.78–16.0); and for the one patient with 'other' functional disorder 7.74. The lack of any statistical differences in the VBRs between the major psychoses is supported by Jeste *et al* (1988).

In 1965, 21 of these 23 patients were graded as dyskinesia negative. By 1981, 12 patients had developed dyskinesia (eight mild and four moderate). All P values in the following analyses are one-sided.

The mean VBR of the 11 patients who remained dyskinesia negative in 1965 and 1981 was compared with the mean ratio of the 12 who became mild and moderate dyskinesia positive. Age was corrected for on a linear basis. The VBRs were significantly larger in the dyskinesia-positive group (13.82 compared with 11.65, $P = 0.052$). A similar difference was obtained, 14.44 compared with 11.78 ($P = 0.061$), if the mild cases were excluded, leaving only the four cases of moderate severity. When the 19 nil and mild cases of facial dyskinesia were combined and then compared with the moderate cases the difference in means was reduced to a comparison of 14.75 with 12.82, which was not statistically significant.

As expected, there was a highly significant correlation between VBR and age ($r = 0.670$, $P = 0.01$).

The correlation between dementia score and subjective age error was $r = 0.50$ ($P = 0.012$). With linear corrections for age, the correlation between (a) brain scan scores and total dementia score was $r = 0.53$ ($P = 0.007$), and (b) brain scan scores and subjective age, $r = 0.38$ ($P = 0.044$).

The relationship of neuroleptic treatment to VBR was evaluated using regression analyses. The only neuroleptic item having a statistically significant association with high VBRs was "total amount of neuroleptics" (Table 3).

Table 2
Facial dyskinesia in 99 non-organic survivors in 1965 and 1981

Age in 1981	Total	Dyskinesia present in 1965	Dyskinesia present in 1981
<50 years	16	1 (6.25)	2 (12.5)
51–60	17	1 (5.9)	9 (52.9)
61–70	25	3 (12.0)	9 (36.0)
Over 70	41	13 (31.7)	26 (63.4)
Total	99	18 (18.4)	46 (46.5)

Figures in parentheses are percentages of total.

Table 3
Statistical association between VBRs and "total amount of neuroleptics" allowing for other variables

		P
(1)	Total amount neuroleptics + linear age	0.004
(2)	As (1) + effect of major affective disorder relative to schizophrenia	0.005
(3)	As (2) + effect of 'schizoaffective and other' relative to schizophrenia	0.031
(4)	As (3) + length of illness	0.053
(5)	As (4) + interaction of length of illness with psychiatric diagnosis	0.017

Total $n = 23$.

Discussion

The present study has limitations (a–e).

(a) Only facial dyskinesia was assessed. However, though the body distribution of dyskinesia may reflect important variants (Glazer *et al*, 1988; Gureeje, 1989), facial dyskinesia is the commonest variant, being found in 81% of cases of dyskinesia (Jeste & Wyatt, 1982).

(b) Dyskinesia may vary considerably, depending on factors such as drug dosage and emotional state. Dyskinesia ratings are also liable to lack consistency between observers and can fluctuate spontaneously (Bergen *et al*, 1984; Gardos *et al*, 1988). Such reservations are less important when deciding whether dyskinesia is absent or present, or whether it is of the more severe grades. That one investigator (HAMcC) took part in the assessments both initially and at follow-up 16 years later helped ensure consistency in the ratings. Furthermore, in both 1965 and 1981 ratings were by extended observations and by consensus of two investigators, thus reducing the chances of observer error.

(c) No interim examinations were carried out between 1965 and 1981 and the hospital case records were too unreliable to date the onset or change in dyskinesia severity.

(d) The drug items used in the analyses are based on five-year checks only during follow-up.

(e) This study is based on a population of patients who survived 16 years from first examination. The results will not necessarily relate to all patients, and any inferences made about this population must be based on medical arguments rather than statistical inference. An important bias is that the majority of patients in the original 1965 study had died before follow-up. Our mortality study (McClelland *et al*, 1986) found a significant association between diminished life expectancy and facial dyskinesia, allowing for age and psychiatric diagnosis.

To set against these shortcomings the Newcastle study had a lengthy (16-year) follow-up and neuroleptic data extending up to 10 years before 1965. This lessens the problem inherent in a non-dyskinetic control group, namely, when a population is taken into a group at a particular stage, there are an unknown number of patients who, although initially dyskinesia negative, will develop dyskinesia. In this study the patients who were non-dyskinetic after a 16-year follow-up period can be considered to be comparatively dyskinesia-resistant and this will highlight differences between the groups.

The prevalence and course of facial dyskinesia

In the 99 survivors with no organic brain syndromes, the prevalence of dyskinesia had risen during follow-up from 18.4% to 46.5% (17 cases out of the 46 being moderate or severe). This is a substantial increase, even allowing for the follow-up population being 16 years older. The over-50 age group was more vulnerable, as has been found in other studies.

Our prevalence rate is similar to that of Bell & Smith (1978) who, in their survey of 1329 patients, found an overall prevalence of 40% (12% severe and 26% moderately severe). Jeste & Wyatt (1982) reported a steady increase in the prevalence of tardive dyskinesia, with the mean prevalence of 12 studies published over 1976–80 being 25.6%. They argued that this was a real increase and not due to increased awareness by physicians, but the prevalence rate may have reached a plateau with the implication that some patients are resistant to dyskinesia. Our results suggest that, if a plateau exists, it is higher than that calculated by these authors. Our findings are more in agreement with a three-year follow-up study of facial dyskinesia (Barnes *et al*, 1983), which found an increase in prevalence in 99 patients from 39% to 47%.

It is probable that tardive dyskinesia may occur in any psychiatric disorder but patients with affective disorder are now recognised as a high-risk group (Gardos & Casey, 1987). Our findings showed the lowest prevalence (43.5%) of dyskinesia in schizophrenia, with schizoaffective and affective disorders having higher frequencies (53.3% and 52.9% respectively). Why there should be this high dyskinesia prevalence when an affective component is present is unclear.

Six of the 14 patients with dyskinesia in 1965 became dyskinesia-free by follow-up – a remission rate of 43%. Three of the six had remained on neuroleptics throughout. These numbers, though small, suggest that for long-term survivors dyskinesia is not inexorably progressive, a finding consistent with the Task Force report of the American Psychiatric Association (1980). Barnes *et al* (1983) in their three-year follow-up study found a remission rate of 36%. A study on the natural history of tardive dyskinesia (Gardos *et al*, 1988) found statistically significant improvement in tardive dyskinesia scores at four years followed by a tendency to deterioration. All studies emphasise the fluctuating nature of tardive dyskinesia.

The trend for Parkinsonism to be associated with the development of later dyskinesia may suggest an inherent vulnerability of the basal ganglia. Jeste & Wyatt (1982) argued there was no satisfactory evidence that early Parkinsonism predisposed to tardive dyskinesia. However, since then prospective studies (Kane *et al*, 1986; Chouinard *et al*, 1986) have given good evidence that early extrapyramidal symptoms are a risk factor.

Treatment factors and dyskinesia changes

The items 'total amount of neuroleptics', 'increasing amount of neuroleptics', and 'total duration of neuroleptics' were significantly associated with the development of dyskinesia. Despite general acceptance that the majority of dyskinetic movements are neuroleptic-induced, many studies have been unable to find any significant association (Casey, 1987). However, most studies have been cross-sectional in design, depending on retrospective spanning of unsystematically recorded pharmacological data and this, combined with uncertainty about when the dyskinesia began, makes it difficult to determine the role of medication. It is noteworthy that the eight patients who never received neuroleptics remained dyskinesia-free, except for one who developed mild facial dyskinesia.

There was no evidence that lithium, benzodiazepines, antidepressants, ECT, psychosurgery or insulin coma carried an increased risk for the development of facial dyskinesia. Anti-Parkinsonian drugs were significantly associated with the development of dyskinesia, but their use may merely represent attempted control of Parkinsonism.

Dyskinesia, CT scans, cognitive impairment, neuroleptic prescribing

There is increasing evidence that dyskinesia, abnormal brain structure and cognitive impairment are associated with one another. Waddington (1987), while acknowledging that results could be conflicting, concluded that cognitive impairment – and the defect state – were present to a greater extent in patients with involuntary movements than in those without; he also concluded that dyskinesia was associated with enlarged ventricles.

These conclusions are given some support by our findings. Development of dyskinesia was significantly associated with enlarged ventricles, with age corrected for. Cognitive impairment was significantly associated with enlarged ventricles and also showed an association with development of dyskinesia. Cognitive impairment was also significantly associated with longer duration of schizophrenic illness, suggesting a deterioration in time, although it could be that such illnesses were intrinsically more severe from the onset than those of shorter duration.

Given this association of dyskinesia, enlarged ventricles, and cognitive impairment, and bearing in mind the now established role of neuroleptics in causing dyskinesia, the question may be asked whether these drugs have wider neurodegenerative manifestations. Wilson *et al* (1983), on the basis of clinical observations, have invoked the concept of "tardive dysmentia", a syndrome with affective and behavioural changes due to neuroleptics, while Goldberg (1985) has postulated an iatrogenic (neuroleptic) frontal lobe dysfunction superimposed upon an intrinsic disease process. One study found a significant correlation between dyskinesia, cognitive impairment and abnormal brain scans, and the authors suggested, but could not confirm, an aetiological role for neuroleptics (Famuwiya *et al*, 1979). However, a study (Owens, 1985) of 110 patients with and without dyskinesia showed no relationship between VBR and past neuroleptic experience. Shelton & Weinberger (1986), in a review, found no relationship between degree of ventricular dilatation and extent of neuroleptic treatment.

In conclusion, our study has found a significant association between neuroleptic prescribing and dyskinesia development and also with ventricular enlargement. The long-term predicted prevalence of dyskinesia for female patients with no primary or secondary organic brain syndromes on neuroleptics may well be of the order of 40–50%. Dyskinesia is associated with reduced life expectancy, and all patients who had severe dyskinesia in 1965 had died by the time of follow-up.

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A Comparison of the Withdrawal Responses of Heroin and Methadone Addicts during Detoxification

MICHAEL GOSSOP and JOHN STRANG

This study compares the withdrawal responses of methadone and heroin addicts during a ten-day in-patient detoxification programme with methadone. Contrary to suggestions in the literature, the methadone group reported more severe withdrawal symptoms during both the acute withdrawal phase and the recovery phase. There were no differences between the two groups in onset or duration of symptoms. Whereas there may be reasons to favour methadone as a maintenance drug, its use may lead to difficulties during withdrawal.

One of the most widely used methods of withdrawal for opiate addicts involves gradually reducing doses of oral methadone. It has been suggested that as many as 10 000 opiate addicts may be withdrawing on methadone at any one time in the US (Kleber *et al*, 1980). Where users are dependent upon heroin, methadone is substituted for the heroin before withdrawal, and then reduced, usually over 10–21 days. This procedure has had considerable success when applied in an in-patient setting and previous studies have reported that more than 80% of opiate addicts completed this sort of detoxification programme (Gossop *et al*, 1986; Gossop *et al*, 1989*a*).

Vogel *et al* (1948) suggested that withdrawal from methadone was likely to be less severe but more prolonged than withdrawal from morphine. This view of methadone's withdrawal effects is widely accepted. For example, Jaffe (1985) states that the methadone withdrawal syndrome is "qualitatively similar to that of morphine, but it develops more slowly and is more prolonged, although usually less intense"; he also suggests that methadone withdrawal symptoms are remarkably persistent and that as much as three weeks may elapse between the peak of withdrawal and the point at which symptoms begin to subside. Detailed investigation of the opiate withdrawal syndrome in response to methadone detoxification programmes has confirmed that residual withdrawal symptoms persist well beyond the last day of methadone administration (Gossop *et al*, 1987, 1989*b*). However, it is interesting that many addicts believe that withdrawal from methadone is more severe than from heroin, and users commonly report that withdrawal from methadone is in some sense 'worse' than that from heroin (Stewart, 1987). Robertson (1987) comments that the methadone withdrawal symptoms are "of a more severe nature than those associated with heroin". Bone pains and muscular aches are prominent adverse effects attributed to methadone by addicts, some of whom may even prefer an unmodified withdrawal from heroin to a short-term methadone detoxification (Hunt *et al*, 1986).

Heroin and methadone have both been used in the treatment and management of opiate addicts in the UK although, in practice, heroin has only been used in a very small number of cases. In recent years there has been a revival of interest in the possible uses of heroin. Ghodse *et al* (1990) reported on the double-blind use of either heroin or methadone during the dose-assessment phase before the in-patient detoxification of opiate addicts, and suggested that heroin addicts required more frequent doses of heroin during a stabilisation phase before detoxification. However, there have been no direct clinical comparisons of the relative severity or persistence of withdrawal symptoms when coming off heroin or methadone. The present study compares the responses of heroin and methadone addicts during a ten-day gradual methadone reduction schedule.

Method

The subjects in this study were 83 consecutive admissions (60 men, 23 women, mean age 27.9 years) to an in-patient drug treatment unit and all were physically dependent on opiates, as confirmed by the presence of morphine metabolites or methadone in urine analysis, and by clinical examination.

Subjects were divided into a heroin and a methadone group according to their pre-admission type of opiate use. Forty-five subjects were categorised as being exclusively or primarily dependent on heroin (either illegally obtained, or prescribed) and 38 subjects as exclusively or primarily dependent on methadone. In 47 cases, subjects used only one type of opiate (heroin $n = 37$, methadone $n = 10$). It is common for addicts to use more than one type of opiate drug. In those cases where subjects used both heroin and methadone ($n = 36$), subjects were allocated to groups according to their major type of opiate dependence (defined by dose, and using the dosage conversion procedures suggested by Banks & Waller (1988)). Doses of methadone ranged from 10 mg to 105 mg (mode of 60 mg) per day.

Total daily opiate doses before admission were calculated by converting methadone doses into heroin equivalents (as above). As there are many problems associated with any attempt to achieve an accurate formula for such conversions, some of which have been discussed by Johns & Gossop (1985), no attempt was made to express heroin and methadone doses in directly comparable and quantitative terms. However, it was felt important to obtain some index of dose. For this reason, the total daily opiate dose of the subjects (i.e. heroin plus methadone for those who used both drugs) was calculated in terms of dose categories, and non-parametric rather than parametric statistics were used in the analysis of data regarding dose categories. Subjects were divided into three dose categories: group 1, less than ½ g ($n = 35$), group 2, ½–1½ g ($n = 22$), group 3, more than 1½ g ($n = 26$). There was no difference between the methadone and heroin groups in pre-admission total opiate dose levels ($\chi^2 = 0.49$, $P = 0.82$, NS).

All subjects received a ten-day supervised in-patient methadone withdrawal. This involved daily reductions from an individually tailored starting dose of methadone which had been established during the first three days after admission, when the patients were given a 'trial' dose of methadone based mainly upon self-reported opiate use, and this dose was then titrated according to clinical observation of their responses. In this study, two measures were taken of the subjects' opiate dose. The first was self-reported daily opiate use before admission; the second was the initial withdrawal dose of methadone prescribed at the start of the ten-day detoxification procedure. This detoxification phase was the first stage of a more comprehensive treatment package and was not offered as a treatment in its own right: all subjects were encouraged to remain in hospital for a treatment package lasting for approximately 8–10 weeks.

Withdrawal responses were measured by means of the 12-item Short Opiate Withdrawal Scale (SOWS). This self-rating scale was specifically devised for the measurement of opiate withdrawal symptoms. Both in its longer (32-item) version and in its present form, the total withdrawal score provides a reliable and valid measure of the opiate withdrawal syndrome (Bradley *et al*, 1987; Gossop, 1990). The 12 SOWS items, each of which was rated on a four-point scale (0 – nil, 1 – mild, 2 – moderate, 3 – severe) were: (a) feeling sick/nausea, (b) stomach cramps, (c) muscle spasms, (d) feelings of coldness, (e) gooseflesh, (f) heart pounding, (g) muscular tension, (h) aches and pains, (i) weakness, (j) yawning, (k) runny eyes, and (l) problems sleeping/insomnia. The SOWS were administered to all subjects at admission and every second day during and after detoxification, for 23 days.

Results

The overall detoxification completion rate was 84% (70/83 subjects). This is comparable to that reported in other studies at this unit (Gossop *et al*, 1989*a*,*b*). There was no difference between the heroin and methadone subjects in terms of either detoxification completion rates ($\chi^2 = 0.0$, $P = 1.0$, NS) or in terms of total length of stay on the unit (31 days and 40 days respectively; $t = 1.54$, $P = 0.12$, NS).

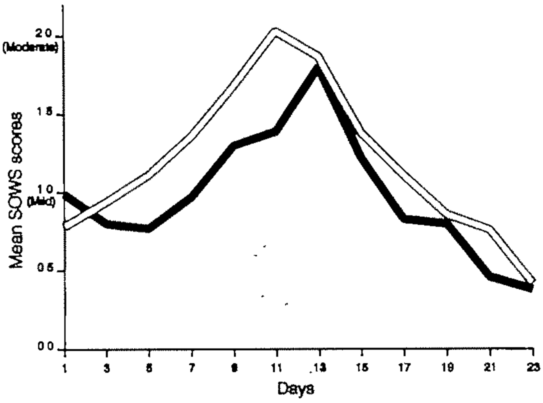

Fig. 1 Mean SOWS scores (methadone (□) and heroin (■) addicts) during withdrawal of methadone (days 1–10) and subsequently.

The means of the total SOWS scores for the two groups were compared during the acute withdrawal phase (days 1–13) and during the recovery phase (days 14–23). The methadone group showed significantly higher levels of withdrawal symptoms both between days 1 and 13 ($t = 3.39$, $P < 0.001$), and between days 14 and 23 ($t = 2.20$, $P < 0.05$). This effect was more evident during the acute phase (days 1–13) (Fig. 1). In order to investigate this effect in more detail, comparisons were made of the contribution of the individual symptom scores to the total SOWS score. During the acute phase there were statistically significant differences between the two groups on 8 of the 12 symptoms, and methadone subjects reported higher symptom levels on all items. These symptom scores with the t values for the group comparisons and the levels of statistical significance are shown in Table 1. The mean dose of oral methadone prescribed to subjects in the methadone group at the start of the detoxification programme was higher than that prescribed for subjects in the heroin group (59 mg and 50 mg respectively, $t = 3.27$, $P < 0.001$). Correlation coefficients were calculated between the peak severity of withdrawal symptoms at the end of the

Table 1
Mean differences between 45 heroin addicts and 38 methadone addicts on SOWS symptom scores

Item	Heroin	Methadone	t	P
Feeling sick	0.9	1.1	2.55	<0.05
Stomach cramps	1.1	1.3	1.39	NS
Muscle spasms	1.0	1.3	2.84	<0.01
Coldness	1.4	1.6	1.79	NS
Gooseflesh	1.2	1.3	1.27	NS
Heart pounding	0.7	0.8	1.13	NS
Muscular tension	1.2	1.6	3.40	<0.001
Aches and pains	1.3	1.6	3.13	<0.01
Weakness	1.3	1.6	3.23	<0.001
Yawning	1.0	1.2	2.32	<0.05
Runny eyes	0.7	0.9	2.41	<0.05
Insomnia	1.2	1.7	4.74	<0.001

ten-day methadone programme and the initial withdrawal dose, and between peak withdrawal scores and the total dose of opiates used before admission. There was no statistically significant relationship between peak withdrawal scores and initial withdrawal dose; nor was there any significant correlation between peak withdrawal scores and prior opiate dose (both correlation coefficients calculated for days 11 and 13).

Discussion

Our results show that methadone addicts report more severe withdrawal responses than heroin addicts during an in-patient gradual methadone reduction programme. The methadone group had more severe withdrawal symptoms, as measured by the SOWS, during both the acute phase of detoxification (up to day 13) and the recovery phase. This difference, which was more marked during the acute phase of withdrawal, cannot be attributed to a dosage effect. Neither the dose of opiates used before withdrawal nor the initial withdrawal dose were related to peak withdrawal severity, and there was no difference between the heroin and methadone groups in terms of daily opiate use before admission. However, the methadone group received higher doses of methadone during detoxification and, therefore, might have been expected to have had a less severe withdrawal response due to the greater pharmacological cover. These results do not support previous suggestions that withdrawal from methadone is less severe than that from heroin (Vogel *et al*, 1948; Jaffe, 1985).

Similarly, we found no difference in either the onset or decay of symptoms for the two groups. The withdrawal syndrome appears, develops and declines at the same rate for both the heroin and the methadone addicts. The only minor difference suggested by our results is that the peak occurs on day 11 (the first day of abstinence after detoxification) for the methadone addicts, and on day 13 for the heroin addicts. It is unclear why this should occur. This similarity in the withdrawal syndrome associated with the two drugs is contrary to suggestions that the methadone withdrawal syndrome has a slower onset, and that it is more prolonged than that from heroin (Vogel *et al*, 1948; Jaffe, 1985; Robertson, 1987). However, since the two groups in this study included a number of subjects who used more than one type of opiate, further research might look at whether or not the same effects are seen with samples of heroin-only and methadone-only subjects. In view of the fact that certain selection processes would operate with such 'pure' samples (e.g. programme-entry criteria and programme-compliance effects for subjects receiving methadone only on a prescription) any research would need to control for such factors.

There has been a revival of interest in the prescribing of maintenance drugs to opiate addicts and current policy looks more favourably on the prescribing of methadone in this context (Royal College of Psychiatrists, 1989). Whereas there may be reasons to favour methadone as a maintenance drug, our results suggest that special difficulties may arise during the withdrawal phase of treatment as a result of the prior substitution of methadone for heroin because of the greater severity of its associated withdrawal syndrome.

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Interictal Psychopathology in Epilepsy
Prevalence and Pattern in a Nigerian Clinic

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An unselected sample of 204 epileptic patients attending a neurological out-patient clinic in Abeokuta, Nigeria, was evaluated for psychiatric morbidity using the CIS. Thirty-seven per cent emerged as psychiatric cases, almost a third of these being cases of psychosis. Patients with partial seizure of temporal lobe origin were the most psychiatrically impaired, while those with partial seizure of non-temporal lobe origin the least. These findings are broadly similar to those reported for epileptic populations in other studies. However, in spite of the relatively high prevalence of major psychiatric disorders among these patients, their impairments were more likely to remain 'hidden' and untreated than those in similar patients in developed countries.

Even though it is widely accepted that there is an increased psychiatric morbidity among patients with epilepsy, methodological differences have ensured limited comparability of the results of most prevalence studies. Until fairly recently, widely accepted criteria for the diagnosis of the various forms of epilepsy were not available. It was, therefore, difficult to be sure that, for example, 'temporal lobe epilepsy' in one study described the same clinical entity as in another. Also, the identification of psychiatric morbidity among epileptics was commonly conducted without the use of standardised instruments and psychiatric diagnoses were often made without reference to any standard criteria. Even when standardised instruments, such as personality inventories, were used, their appropriateness to the population and the problems being assessed was sometimes open to question (Bear & Fedio, 1977). It is, therefore, little wonder that inconsistencies frequently emerged from studies of the prevalence of psychiatric morbidity in epileptic patients and in the association of specific types of epilepsy with psychiatric morbidity (Pond & Bidwell, 1959; Slater *et al*, 1963; Small *et al*, 1962; Stevens, 1966; Currie *et al*, 1971).

In recent years, attempts have been made by some authors to improve on the methodology of previous studies by the use of well defined criteria for the diagnosis and subtyping of epilepsy, and standardised interviewing techniques for the detection of psychiatric morbidity among epileptics (Edeh & Toone, 1987). Such studies ought to be repeated in diverse cultural settings because of the likelihood that the prevalence and pattern of psychiatric morbidity among patients with epilepsy may in part be related to cultural attitude to the disorder.

The study of the prevalence and pattern of psychiatric disorders among epileptic patients in developing African countries has an added significance in view of the high prevalence of epilepsy in these countries. While prevalence figures for epilepsy of 0.4–0.5% have often been quoted for developed nations (Kurtzke & Kurland, 1973), figures ranging between 2.9% and 4.9% have been reported in some epidemiological studies conducted in black Africa (Osuntokun *et al*, 1982; Gerritis, 1983; Gousmit & Van der Waals, 1983). This tenfold increase in prevalence may be related to the poor obstetric care available in these developing countries, in which case many more of such patients than those from developed countries may have underlying brain damage resulting from perinatal complications. Differences in the incidence of brain damage may produce a differing pattern of psychopathology among such patients since a number of authors have noted a relationship between the development of psychosis by epileptics and underlying brain damage (Slater *et al*, 1963; Kristensen & Sindrup, 1978*a*,*b*).

With a few exceptions (Asuni & Pillutla, 1967; Odejide & Bademosi, 1976), systematic studies of the psychiatric sequelae of epilepsy in black Africans are generally lacking. Earlier studies were beset with the methodological problems described above and therefore can no longer be used for comparative purposes.

The aim of the present study was to systematically screen for psychiatric morbidity an unselected population of epileptic patients, whose primary disorder had been rigorously diagnosed. The patients were all attending a neurological out-patient clinic where most of the psychiatric morbidity had not been previously detected. The study aimed at establishing the pattern of this morbidity especially with regard to the currently accepted subtypes of epilepsy.

Method

The study was conducted in the Neurology Clinic of the Aro Neuropsychiatric Hospital, Abeokuta, Nigeria. The clinic operates an open-door policy with most of the patients being either self-referred or brought by relatives. Only a few of the new patients at the clinic had received any form of orthodox medical care for their illness before presenting at Aro. Treatment was therefore instituted at this clinic and follow-up care provided. Also, except for patients in need of other specialist care (e.g. neurosurgical intervention), no referrals were routinely made to other centres for the management of epilepsy. Thus, the patient population in the clinic was essentially unselected. The clinic was run weekly in rotation by a team of five consultant neurologists, two of them being paediatric neurologists. All were consultants at the University College Hospital, Ibadan.

Whether attending for the first time or for a follow-up visit, every clinic attender who met the selection criteria was screened by the author for psychiatric morbidity. However, no one was screened more than once.

Patients were included in the study if: (a) they were aged 13 years or over; (b) a definite diagnosis of epilepsy had been made by one of the consultant neurologists; and (c) there was no evidence of mental subnormality or other gross diagnosable neurological disorder.

The assessment continued until 204 patients, the desired sample size, had been evaluated. A 16-channel electroencephalography (EEG) was conducted on all patients. The recordings were visually assessed by either an experienced neurophysiologist or a consultant neurologist. Computerised tomography was not available in the hospital.

Using a combination of clinical and EEG considerations, the type of epilepsy was determined along the lines described in the modified version of the international classification of epilepsy (ILAE, 1981). Thus three main divisions were encountered as follows.

(a) Primary generalised epilepsy (PGE) in which there was no localising pre- or post-ictal event, and no focal neurological signs. The EEG, when abnormal, was characterised by paroxysmal bursts of high-voltage polyspikes and irregular slow-wave activity occurring in a bilaterally synchronous fashion (Solomon, 1967).
(b) Partial seizures of temporal lobe origin (TLE) with EEG recordings showing the presence of spikes, sharp waves and phase-reversals over the anterior or mid-temporal areas (Ervin, 1967; Driver, 1970).
(c) Partial seizures of non-temporal lobe origin (partial non-TLE) with elementary symptoms and non-temporal EEG focus.

Psychiatric assessment was conducted using the Clinical Interview Schedule (CIS; Goldberg *et al*, 1970), a standardised, semistructured inventory designed for use among respondents who may not see themselves as psychiatrically disturbed. Its feasibility and reliability have been demonstrated in diverse cultural settings (Goldberg & Blackwell, 1970; Mari & Williams, 1984; Dhadphale *et al*, 1983). It has also been used among epileptic patients (Edeh & Toone, 1987), and, in a previous study by the author in the same environment as that of the present study, was found to be acceptable to the respondents (Gureje, 1986; Gureje & Adewunmi, 1988). The CIS assesses 10 reported symptoms in the previous week and 12 abnormalities manifest at interview, each on a five-point scale: 1 for subclinical disturbance or trait, and 2, 3 and 4 for mild, moderate or severe clinical disturbance respectively. A detailed manual gives definitions of all the terms and criteria for rating each of the items. The severity rating which corresponds best with clinical impression is derived by doubling the manifest abnormalities ratings and then adding all the ratings together. A total of 13 and above provides the closest approximation to 'caseness' (Benjamin *et al*, 1982) and, in

Table 1
Characteristics of the patients with primary generalised epilepsy (PGE), partial seizure of temporal lobe origin (TLE) and partial seizures of non-temporal lobe origin (partial non-TLE)

	PGE ($n=99$)	TLE ($n=82$)	Partial non-TLE ($n=23$)
Sex			
male	59	51	13
female	40	31	10
Mean age (s.d.): years	24.6 (10.9)	25.4 (12.9)	22.0 (10.9)
No. (%) with marital status:			
never married	57 (58%)	53 (64%)	17 (74%)
married	36 (36%)	26 (32%)	4 (17%)
separated or divorced	6 (6%)	3 (4%)	2 (9%)
No. (%) in social class			
I–III	23 (23%)	13 (16%)	2 (9%)
IV–V	76 (77%)	69 (84%)	21 (91%)
Mean age of onset (s.d.): years	17.7 (11.2)	18.3 (13.3)	14.2 (10.3)
Mean duration of epilepsy (s.d.): years	6.8 (4.9)	7.1 (5.8)	7.8 (7.0)
No. (%) with frequency of fits:[1]			
one or more per month	53 (46%)	51 (62%)	4 (17%)
less than one per month	46 (46%)	31 (38%)	19 (83%)
No. with no. of drugs prescribed:			
one	98	81	22
two	1	1	1
No. (%) with history of birth difficulties:			
no	67 (68%)	48 (58%)	18 (78%)
yes	4 (4%)	8 (10%)	2 (9%)
unknown	28 (28%)	26 (32%)	3 (13%)
No. (%) with history of childhood medical problems:			
no	47 (48%)	26 (32%)	7 (30%)
yes[2]	30 (30%)	39 (47%)	14 (61%)
unknown	22 (22%)	17 (21%)	2 (9%)

1. $\chi^2=13.86$, d.f. $=2$, $P<0.005$.
2. $\chi^2=8.15$, d.f. $=2$, $P<0.025$.

Table 2
Comparison of the epilepsy groups on CIS items

CIS items	ANOVA[1]		Differences between the groups (Mann–Whitney *U*-test)
	H	*P*	
Reported symptoms:			
impaired concentration	9.414	0.009	TLE v. PGE, $P=0.01$ TLE v. non-TLE, $P=0.04$
depression	6.206	0.045	TLE v. PGE, $P=0.02$
anxiety	9.989	0.007	TLE v. PGE, $P=0.01$
Manifest abnormalities:			
depressed affect	6.035	0.035	TLE v. PGE, $P=0.03$
elated or euphoric	6.133	0.047	Non-TLE v. TLE, $P=0.01$

1. Kruskal–Wallis one-way analysis of variance, corrected for ties.

this study, any subject with such score was given a clinical diagnosis according to ICD-9 (World Health Organization, 1978).

Demographic, perinatal and childhood data and details of seizure were obtained from patients or their close relatives. These were recorded on a proforma based on a modified item sheet published by Taylor & Falconer (1968).

Analysis of data

Results were analysed using the χ^2 test for categorical variables, *t*-test for comparison of means of normally distributed variables and the Mann–Whitney *U*-test for distribution-free continuous variables. Differences among the three epileptic groups were determined using the Kruskal-Wallis one-way analysis of variance. Analyses were performed using the SPSS-PC+ (Version 2.0) program.

Results

The sample consisted of 99 patients with PGE, 82 with TLE, and 23 with partial non-TLE. The three groups had broadly similar demographic features (Table 1). Twenty (9.8%) of the patients were aged less than 15. Of these, 13 had PGE, six had TLE while one had partial non-TLE. There was significantly better control of fits in the partial non-TLE group than in the other two groups. The general practice in the clinic was to attempt to maintain patients on a single drug in order to ensure good compliance. Except in the very few cases of *petit mal* attending the clinic, only two of whom were in the present sample, the first choice of medication was phenobarbitone. Table 1 reflects this practice, showing that only three patients were on two anticonvulsants. As far as could be determined, the three epileptic groups were identical with regard to history of birth difficulties (that is, prolonged labour, forcept extraction, Caesarian section, abnormal presentation, respiratory distress after birth, etc.). However, significantly more patients with partial epilepsies gave a history of childhood physical problems (febrile convulsions, severe exanthemata, known or probable mastoiditis, status epilepticus or head injury leading to admission to hospital before the age of five years).

Table 2 shows the comparison of the three groups with regard to their mean scores on five of the CIS items (three reported symptoms, two manifest abnormalities). These five items, which significantly differentiated the three groups on testing with the Kruskal–Wallis one-way analysis of variance, were then used to compare the groups in pairs using the Mann–Whitney *U*-test. As can be seen in Table 2, the TLE group rated as more highly impaired on four items than the PGE group and on one item than the partial non-TLE groups. On manifest elation or euphoria the partial non-TLE group rated as more disturbed than the TLE group.

Table 3
Distribution of psychiatric disorders

Diagnoses	Primary generalised		TLE		Partial non-TLE	
	n	%	*n*	%	*n*	%
Normal	66	67.0	42	51.0	20	87.0
Neuroses:	19	19.0	20	25.0	1	4.0
depressive neurosis	(8)		(10)		(–)	
anxiety	(8)		(8)		(1)	
phobic state	(–)		(2)		(–)	
hypochondriasis	(2)		(–)		(–)	
obsessional neurosis	(1)		(–)		(–)	
Psychoses:	6	6.0	15	18.0	1	4.0
schizophrenia	(4)		(13)		(1)	
organic psychosis	(2)		(–)		(–)	
paranoid psychosis	(–)		(1)		(–)	
depressive psychosis	(–)		(1)		(–)	
Personality disorders:	8	8.0	5	6.0	1	4.0
epileptic personality	(6)		(2)		(1)	
hyperkinetic conduct disorder	(–)		(3)		(–)	
explosive personality	(1)		(–)		(–)	
antisocial personality	(1)		(–)		(–)	
Total	99	100.0	82	100.0	23	100.0

For differences between major categories: $\chi^2=14.87$, 6 d.f., $P<0.025$.

The mean (s.d.) total scores for the groups were: PGE, 6.55 (8.28); TLE 10.71 (10.47); and partial non-TLE 4.25 (5.20). The difference between the PGE and TLE groups was statistically significant ($Z = -2.735$; $P = 0.006$).

The frequency and type of psychiatric disorders are shown in Table 3. While patients with TLE were the most psychiatrically impaired, almost half of them having one type or the other of psychiatric impairment, those with partial non-TLE seizures were the least impaired.

The difference between the three epileptic groups with regard to the prevalence of psychiatric disorders was statistically significant ($\chi^2 = 14.87$, $P < 0.025$). Neurotic disorders were by far the commonest forms of psychiatric disorders, accounting for about 53% of the total morbidity. Most of these cases were of anxiety or depressive neurosis.

About 29% of the total morbidity was accounted for by various psychotic disorders. Here, patients with TLE were the most disturbed, constituting about 68% of such cases. Schizophrenia-like psychoses were the commonest diagnosis. Four of the 18 patients with this diagnosis had prominent depressive symptoms that would perhaps qualify them for a label of schizoaffective disorders. In all, nine of the 18 patients with schizophrenia had at one time or other received orthodox psychiatric treatment before the index evaluation. The two cases of confusional psychosis were precipitated by status epilepticus.

Fourteen (7%) of the patients had personality disorders. Nine of them showed the symptom constellation for which the label of epileptic personality is frequently applied. Such symptoms include apathy, irritability, 'wooliness' of thought and narrowness of field of interests. Such a diagnosis was more common among patients with PGE.

Apart from nine of the patients with schizophrenia and a boy with phobia of darkness, only two other patients gave a history of previous psychiatric referral: one had a diagnosis of explosive personality disorder, and the other had antisocial personality disorder.

Among the 20 patients who were aged less than 15, three had schizophrenia, two behaviour disorder, and one each phobic anxiety and epileptic personality. This represented a 35% prevalence rate of psychiatric morbidity in this age group.

In order to further explore the relationship of the psychiatric impairments to age, a correlational analysis was done between age and the CIS items. Table 4 shows significant correlations. On reported symptoms, irritability was negatively correlated with age. On manifest abnormalities, being slow and lacking in spontaneity was negatively correlated with age, while being excessively concerned with bodily functions was associated with increasing age.

Table 4
Correlation of age with CIS items

CIS item	*r*	*P*
Reported symptom:		
irritability	−0.256	0.001
Manifest abnormalities:		
slow, lacking in spontaneity	−0.217	0.01
excessive concern with bodily function	0.211	0.01

Discussion

The patients in this study differ in important ways from those in some previous studies, especially those from Western countries. They were considerably younger at index assessment, younger at onset of epilepsy, and had a much shorter duration of illness than the samples studied by Kogeorgos *et al* (1982) and by Edeh & Toone (1987). Indeed, in the present sample, as many as 43% of the patients were aged between 12 and 20 years and 9.8% were less than 15 years old. There is evidence that this clinic-derived sample, which suggests an excess of epileptics in the second decade, may be a true reflection of the community pattern (Osuntokun *et al*, 1982).

Another difference between the present and some past studies concerns the proportion of patients on multiple drug treatment. While almost all the patients in the present study were on a single anticonvulsant, about half of the sample studied by Edeh & Toone (1987) were receiving two or more drugs. The intensity of treatment and the age of onset have both been linked to the development of psychiatric morbidity in epileptic patients (Reynolds & Travers, 1974; Scott, 1978). In view of the peculiar problems of the environment where the current study was conducted (e.g. widespread illiteracy, expensive drugs, lack of facilities to monitor drug serum levels, high defaulting rate), the practice in the clinic was strongly influenced by the suggestion of Osuntokun (1979) that drug management of epileptics in developing countries should be made as cheap and as simple as possible.

Even though various methodological differences preclude strict comparisons, the 37.3% prevalence of psychiatric morbidity obtained in the present investigation is higher than the 29% identified by Pond & Bidwell (1959) in their survey of hospital out-patients. However, Edeh & Toone (1987), using case-finding criteria identical to that of the present study, obtained a prevalence of 47.7%. It seems probable that differences in patient characteristics may partly explain this inconsistency. For example, their patients had suffered from epilepsy for a considerably longer period of time and were generally on more intensive treatment as attested to by the proportion on multiple drugs. Their study was also conducted among general practice attenders.

The observation of a greater prevalence of psychiatric disorders in patients with TLE than those with PGE is identical to those of many previous investigators (Flor-Henry, 1969; Shukla *et al*, 1979; Edeh & Toone, 1987). Even though a few authors have disputed this claim, especially with regard to psychotic manifestations (Small *et al*, 1962; Stevens, 1966), the inconsistencies probably result from differences in sampling procedures. The observation of relatively rare psychiatric complications in patients with partial non-TLE is also in line with those of many other studies (Gibbs, 1951; Juul-Jensen, 1964; Sherwin *et al*, 1981). This is, however, dissimilar to Edeh & Toone's (1987) observation of an identical rate of morbidity between patients with temporal lobe epilepsy and those with other foci for their partial seizures.

In spite of this difference and the higher mean total scores of their epileptic groups on the CIS, it is noteworthy that Edeh & Toone's (1987) results were broadly similar to those of the present study with regard to the comparison of the epilepsy groups on the CIS items. Not only were many of the differentiating items identical, the direction of the differences were also very similar.

The precipitation of confusional psychosis by status epilepticus is well reported (Dongier, 1960; Flor-Henry, 1969, 1972; Shukla *et al*, 1979). Also similar to the reports of some earlier investigations are the findings in this survey of a higher prevalence of personality disorders in general, or the symptom constellation referred to as epileptic personality in particular, among patients with PGE (Shukla *et al*, 1979; Edeh & Toone, 1987). However, there are also inconsistencies with regard to these findings as a number of investigators have observed more personality abnormalities among patients with temporal lobe epilepsy (Pond & Bidwell, 1959).

An issue that is not often addressed in studies conducted among epileptics concerns the relationship between psychiatric morbidity and the age of the patients. In their follow-up study of children with TLE, Ounsted & Linsay (1981) found that, at entry into the study only 15% of the children did not show some form of psychiatric morbidity, whereas in adulthood 70% of the survivors had no psychiatric symptoms whatsoever. In the present study, the 35% prevalence rate of any psychiatric disorder among those aged less than 15 years is not dissimilar to the 37% obtained for the entire study population. However, at the individual CIS-item level, significant associations were noticed with age. This observation needs replication. Meanwhile, future research in this area should consider age as an important variable in any description of the morbidity pattern among epileptics.

It is difficult to speculate on the reason for the greater prevalence of psychiatric morbidity among patients with TLE when compared with the other two epileptic groups. The three groups had identical exposure to anticonvulsant medication. Even though the group with TLE had the worst seizure control, the difference between this group and the PGE group with regard to this feature is not significant and is unlikely to account for the sharp contrast between them concerning psychopathology. Also, even though many more patients with TLE than with PGE gave a positive history of childhood medical problems, so did patients with partial non-TLE who were, in this study, the least psychiatrically impaired. In view of some difference between the three groups with regard to the pattern of psychotic morbidities, a more useful question to explore may be that concerning the vulnerability factors for psychopathology within each group. That is, why for example, do some patients with TLE develop psychiatric morbidity while others with the same type of seizure disorder do not?

In general, using present-day criteria for the diagnosis of epilepsy and a standard interview schedule for the identification of psychopathology, this study found a broadly similar range of psychiatric morbidity among this group of African patients as that previously reported from other societies. It was also observed, in line with many other published works, that patients with their epileptic foci in the temporal lobe are particularly at risk for the development of psychiatric morbidity, especially psychotic disorders. However, in spite of these similarities, the patients in this study showed evidence of being at greater disadvantage relative to those reported from Western societies. For example, while as many as 30.7% of Edeh & Toone's (1987) sample had some form of previous psychiatric consultation, only 5.9% in the present sample give such a history of care. This is in spite of the observation that the present sample had a much higher prevalence of major psychiatric disorders than that of Edeh & Toone: 10.8% v. 4.5% prevalence for all psychotic disorders. There is little doubt that this degree of disadvantage is partly related to the paucity of qualified specialists, neurologists and psychiatrists in this environment. Nigeria, with population of about 100 million people and a land area of 356 000 square miles, has less than 100 specialists in the clinical neurosciences.

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Point of View

The Myth of Elevated Serum Creatine Phosphokinase Level and Neuroleptic Malignant Syndrome

ADITYANJEE

The 1980s witnessed the honeymoon between American psychiatry and an enigmatic and mysterious drug complication called neuroleptic malignant syndrome (NMS). I fear that the 1990s are witnessing the same in British psychiatry. Gone is the era when case reports in British literature described the syndrome without identifying it by name (Allan & White, 1972; Moyes, 1973), ostensibly owing to lack of awareness. Probably, no one had bothered to read the original description in the French-language literature (Delay *et al*, 1960). The pendulum has now swung to the other extreme. Every known drug-related complication is being labelled NMS. In the US, Addonizio *et al* (1986) suggested a ridiculously high incidence figure of 12.2%. The same trend for overdiagnosis is seen in the recent case report by Dalkin & Lee (1990). The authors of this case report seem to have forgotten that NMS is an idiosyncratic adverse drug reaction which is dose-independent. There is no reason to label every neuroleptic overdose as NMS on grounds of raised creatine phosphokinase (CPK) level.

Elevation of the serum CPK level is a fairly non-specific phenomenon (Adityanjee *et al*, 1988). Most commonly, an elevated serum CPK level is due to intramuscular injections, use of restraints, or other intense isometric activity (Gabow *et al*, 1982). Acutely psychotic patients are known to have an elevated total CPK level during in-patient treatment (Meltzer *et al*, 1969, 1970). It has also been reported as a result of acute dystonic reactions to antipsychotic drugs (Lui, 1979; Cavanaugh & Finlayson, 1984). The interpretation of an elevated value is often difficult since the level can be elevated in many other clinical situations and also for no apparent reason (Black *et al*, 1986). Black *et al* also found differences in the level of total CPK between men and women and among various racial groups.

Creatine phosphokinase is a sensitive marker of muscle injury. Measurement of serum CPK is routine in the diagnosis of acute myocardial infarction and various muscle disorders (Dreyfus *et al*, 1960; Black *et al*, 1986). A major limitation of CPK measurement is the lack of specificity (Sobel & Shell, 1972; Galen, 1975; Goldberg & Winfield, 1972; Grande *et al*, 1980; Wagner, 1980). False-positive rates as high as 36% for elevated total CPK values have been reported (Grande *et al*, 1978). Many diseases or minor insults can result in leakage of the enzyme into the circulation and raise the serum levels into the abnormal range (Black *et al*, 1986).

Rhabdomyolysis in the absence of NMS can occur as a complication of antipsychotic drugs and may give rise to an elevated CPK level (Ravi *et al*, 1982; Cavanaugh & Finlayson, 1984; Levenson, 1985; Johnson *et al*, 1986). Recently, Pearlman *et al* (1988) described two cases of asymptomatic elevation of CPK after oral neuroleptic treatment. It is not necessary to invoke a diagnosis of NMS in these cases. Levenson (1985), whose diagnostic criteria Dalkin & Lee (1990) have used, described a patient with schizophrenia in whom a misdiagnosis of NMS might have been considered after development of rhabdomyolysis and acute renal failure.

Dalkin & Lee (1990) base their diagnosis of NMS on elevated serum CPK level and state that there are no reports in the literature of neuroleptic-induced dystonic reactions causing a raised CPK level. Before making such a blanket statement the authors might have reviewed the literature on raised serum CPK levels more thoroughly. Neuroleptic overdose in this case seems to have caused muscular rigidity which subsequently improved with procyclidine suggesting it was a dose-dependent extrapyramidal reaction. There is a need for caution while considering the diagnosis of NMS in a patient without fever, since deliberate self-harm through overdose of psychotropic drugs is a very common clinical problem. Otherwise, we would fall into the trap of labelling every neuroleptic overdose as NMS.

Kellam (1990), while discussing the issue of diagnostic criteria for NMS, has touched upon the current controversy. He agrees with Adityanjee *et al* (1988) in surmising that the inclusion of ordinary extrapyramidal reactions to neuroleptics has been responsible for the high incidence of NMS reported from the USA (Kellam, 1990). Diagnostic criteria suggested by Levenson (1985), relying too heavily on elevated CPK level, allow episodes without fever or without muscular rigidity to be characterised as NMS. Later on, Levenson (1986) slightly modified his original criteria and suggested an elevated CPK level as a major manifestation of NMS only when it is more than 1000 U/l. Despite this modification, it is possible to overdiagnose NMS as is illustrated by the case report by Dalkin & Lee (1990). Although the criteria suggested by Adityanjee *et al* (1988) have been considered too stringent (Kellam, 1990; Velamoor *et al*, 1990) they are more realistic in the sense that they minimise the high false-positive rate.

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The Current Literature

Is Sex Necessarily a Risk Factor to Depression?

TIRRIL HARRIS, PAUL SURTEES and JOHN BANCROFT

"To isolate and quantify possible determinants of any increased prevalence of depressive disorders in women we studied a select group of men and women, initially similar in terms of a number of putative social determinants of depression, and reviewed the sample five years later when social role diversity was anticipated. We used the Diagnostic Interview Schedule (DIS) to generate DSM–III and RDC diagnoses to estimate lifetime depressive disorders, and established (via corroborative reports) the likely accuracy of those data. Despite lifetime depression being a relatively common experience, no significant sex differences in depressive episodes were demonstrated, suggesting the possible irrelevance of biological factors in determining any sex difference. As there was not major social role divergence over the five year study, we interpret the lack of a sex difference as a consequence, and suggest that findings support the view that social factors are of key relevance in determining any female preponderance in depression described in general population studies."

The summary quoted above is from an article by Wilhelm & Parker (1989). The present authors were invited to comment upon the study.

Tirril Harris

The most important lesson of this study of sex differences in prevalence of depression is the need for follow-up. 'Wilhelm & Parker Revisited' will, with any luck, be able to answer some of the questions which this first paper has so far been unable to settle, possibly because a five-year follow-up has not been long enough to monitor the evolution of differential role changes between the lives of men and women in young adulthood. Meanwhile, however, the authors deserve credit for the initial design and careful execution of a longitudinal project to examine the possibility that divergences in social and occupational roles are what account for the greater prevalence of depression among women. In 1978, 114 female and 56 male trainee teachers completed state and trait measures of depression, along with the Eysenck Personality Inventory and a dependency scale. In 1983, 109 of these females and all 56 males completed these again, along with the Bem sex-role inventory, before being administered those sections of the DIS dealing with anxiety states and depression to establish lifetime prevalence. This design and sample allowed study of a group who were initially homogeneous in terms of age, marital status, current social class and occupation, but the social role diversity between the sexes anticipated in the succeeding five years was expected to permit a prospective examination of the social-determinant hypothesis.

The results were unfortunately not illuminating in terms of this hypothesis, despite the care shown by the authors in using both RDC and DSM–III diagnostic categories in their analyses, thus enabling comparisons of both minor depression and dysthymia and adjustment disorder. Whether period prevalence before 1978, or between 1978 and 1983, or total lifetime prevalence was examined, there were no significant sex differences. Any trend for a higher pre-intake RDC major depression rate for females was countered by a higher trend for males to develop episodes during the study, so that the lifetime rates were very similar. Nor was there any tendency for women to have longer episodes. On the other hand, nor was there any evidence of sex role divergence: the increased parenthood rate was similar for males and females, and neither the full-time employment rate in 1983 nor the unemployment rate over the interval showed any sex difference. Furthermore, there were no differences between the men and the women on the sex-role inventory.

Despite these negative findings and the failure to document role divergence, the paper is of great value. Firstly, it provides an example of the DIS being thoughtfully used, after a semistructured interview which, at times, addressed depressive experience and highlighted episodes, so that more information was obtained to generate diagnoses than might have been elicited by the DIS alone. Corroborative interviews with nominated witnesses of the depressive episode(s) were achieved for 87% of the subjects interviewed in person (15 had only been contactable by telephone interview), and care was taken to catch these immediately after the subject's own interview, so that 'priming' could not occur. The resulting kappa coefficient of 0.93 for major depressive episodes, and 0.86 for minor ones, gives more faith in their figures than is affordable with reports based on the DIS as it is usually administered. The simultaneous presentation of results in terms of both RDC and DSM–III, and the detailed explanations of how and where these differed, and of the implications of these differences for their conclusions, also brings a refreshing clarity of thought. The discussion section addresses the way in which these usages could have contributed to their considerably higher lifetime rates when compared with other research, especially the Epidemiological Catchment Area (ECA) study (Regier *et al*, 1984). The implication that a semi-structured approach to the administration of the DIS may reveal higher rates of depression (than with its customary structured approach) deserves a much wider audience than merely those interested in sex differences in prevalence.

Secondly, the discussion raises a number of other thought-provoking issues. For example, the trait measures of dependency and neuroticism did show significant sex differences, despite the lack of difference in depression, and the authors use this to underline a theoretical perspective, currently known as the 'vulnerability model' of depression. Here, if dependency and neuroticism are risk factors for depression, they do not by themselves dispose to it, but "require interaction with other disposing (e.g. low social class) or triggering factors (e.g. life events) to precipitate an episode" (p. 411).

Another topic discussed is the possibility of an occupational selection which cuts across the usual range of other predisposing/protecting factors. Thus they suggest that male teachers may be more androgynous than most men, and cite results of a survey of other Australian teachers which suggest that they may also be more liable than men in other occupations to psychological distress (another more feminine characteristic). Certainly the requirements of such a work role have more elements of the feminine or nurturant than most occupations.

Last, and not least, the sample is still being cultivated, and in another decade the postulated sex differences in the independent variables may arise, at which time the hypothesis will be ripe for re-examination. In this connection it may be worth noting some suggestions that could help the authors cope with some of the alternatives which have emerged in the discussion above. On the one hand, despite the development in the future of social role divergence, the postulated sex difference in depression may still not be manifest. One obvious proposal here would be that they incorporate additional measures such as life events, since social role divergence might prove to be only a vulnerability factor whose effects are only clear in interaction with provoking factors, rather than a simple risk factor as such. On the other hand, sex differences in depression may at last emerge with a longer follow-up, but social role divergence still not have developed in their terms.

It would be a pity to waste the opportunity to use such a longitudinal sample to explore some of the other suggested hypotheses for the sex difference – for example that men react with alcohol abuse and other forms of antisocial disorder, while women react with depression – and it is possible they will miss this if they do not extend their measures. (The account of the 1983 data collection suggests they are only looking at depression and anxiety (p. 404).) Other possible variables here, which of course should also differentiate women with and without depression despite their similar social roles, include, among others, liability to pre-menstrual syndrome, oral contraceptive use and ruminative response style (Nolen-Hoeksema, 1987). Finally, it will be important for them to consider how adequately their measures really do encompass the totality of the social role divergence between the sexes: they might believe that the sex difference in depression was arising despite a continuing similarity of roles between the two groups of teachers, but if their measures were not refined enough they might be missing the extent to which these roles really had begun to diverge. Thus the women in the sample might well have the same number of children and the same number of official work hours as the men, but be taking more work home and be spending more hours awake with sleepless children in the middle of the night. Furthermore, they might be receiving less support from their spouses or partners than the men because gender role training predisposes women to be more orientated towards relationships (Gilligan, 1982) and thus better confidants than men. All of these items are likely to contribute to depression and all can be seen as results of social roles differing between the sexes, but it is not clear at the moment how well the authors will be able to document such factors.

Paul Surtees and John Bancroft

This study was designed to seek explanations for the almost universal finding of a gender difference in the rates of affective disorder. Most studies report women to be about twice as likely as men to experience affective illness, whether based upon community or hospital samples (see Nolen-Hoeksema (1987) for a recent review of the evidence).

The design of this Australian study involved two interviews being undertaken five years apart with the assessment of lifetime psychiatric status completed at the *second* interview through use of the DIS. The results concerned the responses from 165 of the 380 students undertaking the course (only 47.1% of the 380 students who agreed to complete a questionnaire designed in part to assess likely compliance in the study). We regard this study as well executed and interesting, but we do have some concerns about the conclusions drawn from the results. Our comments are concerned with two main areas: issues associated with their assessment of the rates of affective disorders, and their view of the role of biological factors in determining sex differences in depression.

The assessment of affective conditions

The DIS, which was used to assess psychiatric status, is a technique developed for the ECA study. Results from this investigation have demonstrated that period prevalence rates of DIS/DSM-III major depressive disorder (MDD) were higher in women than men at *each* of the five study locations and within *every* age group. The Australian results differ therefore from equivalent period prevalence rates obtained in the ECA study. Lifetime prevalence of MDD, based upon a weighted data analysis, across all ECA study areas (for all persons aged 18 years or over) was found to be 4.4%; sex ratios (of one-year prevalence rates) were found to range between 1.9 (in Los Angeles) to 5.0 (in St Louis) and the mean age of onset for DSM-III major depressive disorder was 27.4 years, with no sex difference in age of onset being found (Weissman *et al*, 1988). In the Australian study the overall lifetime prevalence of MDD was found to be 23.0% (by DSM-III criteria), in marked contrast to the ECA rates; e.g. 7.5% found in Baltimore, 8% in St Louis and 10.4% in New Haven for those aged 25–44 years (Robins *et al*, 1984). Little attempt is made in the paper to offer explanation for this considerable difference, the authors suggesting only that their results are "generally comparable" to work other than the ECA. It is clearly important, before generalising from this study, to establish the extent to which this sample, particularly the men, had unusually high rates of affective disorder.

A further point of comparison is to examine the results of broadly similar work undertaken in the southern hemisphere. The Christchurch Psychiatric Epidemiology Study (Wells *et al*, 1989; Oakley-Brown *et al*, 1989), in which a sample of almost 1500 adults aged 18–64 years were given the DIS, provides a basis for such a limited comparison. The Christchurch study obtained a lifetime prevalence rate of MDD for those aged 25–44 years of 15.1% (19.6% for females) and a six-month rate of 5.5% (ratio of rates = 2.75). Further, the female:male ratio of MDD six-month rates (for the same age group) was found to be 3.4 (female rate 8.5%, male rate 2.5%). It would appear therefore that the sex difference in rates was once again demonstrated but that the lifetime rates of MDD were substantially in excess of those found in the ECA, although still not as high as those found in the Australian study.

However, Parker (1987) has commented upon the accuracy of the lifetime prevalence estimates. This sceptical review reflected on the likely validity of the ratio of lifetime to six-month prevalence estimates (of major depression) obtained in the ECA studies. These ratios were of the order of 2 (Weissman *et al*, 1988), indicating that about half of the cases ever rated continued to satisfy or re-satisfied the diagnostic criteria for a major depressive episode during the six months preceding interview. This surprising finding casts doubt on the lifetime prevalence rates obtained in this manner. Such ratios cannot be determined from the Australian paper, and given the limited sample size, it would perhaps be inappropriate to attempt such estimation. However, it remains unclear why the prevalence estimates obtained should differ so widely from those reported by the designers of the DIS.

Wilhelm & Parker also raise the possibility, suggested by others, that the usual sex difference in affective disorders is, at least in part, an artefact of sex differences in symptom reporting. However, a recent report examining sex differences in the lifetime prevalence of depression (Young *et al* (1990), based on over 2000 first-degree relatives of affectively disordered probands of an NIMH collaborative study of depression) refuted this explanation. In particular, the report found that women "had a greater number of associated symptoms only at higher symptom levels, suggesting an excess of women only above a diagnostic threshold". Young *et al* concluded that their results supported a true differential prevalence of major depressive disorder by gender.

The role of biological factors in determining the usual sex differences in depression

In their introduction, the authors comment that, in view of the lack of a sex difference in depression in childhood and advanced old age, the sex difference is greatest during the period when male and female occupational and social roles diverge the most. They appear to overlook the additional fact that the sex difference is greatest when male and female *reproductive* roles diverge the most, that is, during the reproductive phase of a woman's life span. In their discussion, when considering the important point that their teachers represent highly selected and possibly very atypical samples of both men and women, they comment "even if teachers are so idiosyncratic as to have similar rates of psychological morbidity, how can any biological factor imputed as determining sex differences in the general population be over-ridden in such a select group?" The answer is, quite easily. There are few who would seriously contend that factors related to reproductive biology would operate in isolation or without interaction with other sources of influence. Given the emphasis that the authors place on this rejection of biology as a source of explanation, the absence of any attempt to consider how such biological factors might be involved is striking, and out of keeping with the otherwise cautiously critical style of this paper. Let us consider some relevant points.

There are at least four aspects of women's reproductive biology which in general deserve consideration: (a) pregnancy, childbirth and lactation, (b) the menstrual cycle and related mood changes, (c) reactions to steroidal contraceptives, and (d) the menopause and hormone replacement therapy. The first three of these are certainly relevant to the age range of the sample but none received any attention in this report.

A recent study has suggested that the sex difference in depression can be largely attributed to parity in women; the prevalence of depressive psychosis for nulliparous women was found to be very similar (in fact somewhat lower) to that for men (Gater *et al*, 1989). Clearly parity could act in a variety of non-biological ways, but this effect does not appear to be either proportional to the number of pregnancies (Kendell *et al*, 1987), or dependent on having to care for children at home during the day (Bebbington *et al*, 1991). Although parity may have a protective effect in certain social situations (Romans-Clarkson, 1988) and apparently reduces the likelihood of suicide (Veevers, 1973), most of the evidence so far suggests that once a woman has experienced pregnancy she remains *more susceptible* to depression until around the age of the menopause, an effect which is not explained by the occurrence of post-partum depression. (The difference between parous and non-parous women persisted until age 54 in Gater's study and 50 in Bebbington's.) This effect of parity requires explanation, and both biological and non-biological mechanisms could be involved. Wilhelm & Parker report that at the initial assessment, just over 8% of the sample of women were parous and that this had increased to 35.8% at follow-up. However, they did not consider whether the rates of depression were different in the parous and non-parous groups. Furthermore, it would appear that this sample of women is unusual in the low proportion who are parous. Of women born in England and Wales in 1955 (the average year of birth for this cohort), 37% would be expected to be parous at the age of 23 and 70% at the age of 30 (Shaw, 1989), compared with 8% and 36% in the Australian study.

Several studies have shown an association between perimenstrual mood change and depressive illness in women (e.g. Endicott *et al*, 1981; Halbreich & Endicott, 1985). Rubinow *et al* (1986) have suggested that in susceptible women (i.e. women with a predisposition to depressive illness) the repeated challenge to their affective state, month after month, by something analogous to a 'kindling phenomenon', increases the likelihood of a more chronic depression developing. This monthly challenge could depend on neuroendocrine mechanisms, but psychological mechanisms also have to be considered. A woman who experiences this recurrent challenge to her well-being and self-esteem could respond by thinking differently about herself in ways which would perhaps render her more vulnerable to life events. Life-style and occupation may be relevant to this form of vulnerability, as women who are in full-time occupation are less likely to complain of pre-menstrual syndrome (Warner & Bancroft, 1990). Apart from the fact that we know nothing of the prevalence of pre-menstrual mood changes in Wilhelm & Parker's sample of women, it is also distinctly possible that the effects of such recurrent mood change on the incidence of depressive illness, if it occurs, may be maximal in the 30s, and hence not yet fully manifested in this cohort. In considering the possible contribution of biological factors, we should certainly not assume that they will all operate either at the same stage or equally throughout women's reproductive span.

The relevance of oral contraceptive use is in fact difficult to assess. It remains a possibility that oral contraceptives contribute to the development of depression in susceptible women. An unknown but possibly substantial proportion of women discontinue oral contraceptives because of adverse affective reactions. In addition there is some evidence of an increased incidence of depressive illness in women who have used such contraceptives in the past but discontinued them, raising the possibility that women who show these adverse affective responses are susceptible to depressive illness (Bancroft & Sartorius, 1990).

It is rare in epidemiological studies of affective illness (and this Australian report appears to be no exception) for such reproductive variables to receive more than scant attention. Until they do, and produce the appropriate evidence, it is not justified to conclude that women's reproductive biology is irrelevant to the sex difference in depression. It is also arguable whether studies of this kind (e.g. Jenkins (1985), who recruited civil servants), in which groups of men and women are selected on the basis of their social and occupational similarities, resulting in samples which are atypical of either sex, can be expected to throw light on the cause for the almost universally found sex difference in rates of depressive illness. They are informative and of interest in other respects, but as far as the role of biological factors are concerned, a more fruitful approach may be to compare groups of women identified in terms of key aspects of their reproductive biology.

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British Journal of Psychiatry (1991), **158**, 713–722

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Editor: Ian Pullen

Contents: First episode schizophrenia: predicting outcome/Gender-identity clinic patients/Musical and verbal hallucinations/Failure to convulse with ECT/Anorexia nervosa in the elderly/Chronic fatigue syndrome/Family intervention/Uraemia and mania/The social networks of long-term patients/Incestuous abuse in psychiatric patients/Tolbutamide and fatal water intoxication/Tardive oculogyric crisis and obsessional thoughts/Drug-induced koro in a non-Chinese man.

First episode schizophrenia: predicting outcome

SIR: Prediction of outcome following first schizophrenic episode is an area of great importance since clinical practice is likely to be influenced by positive findings, especially if it is suggested that interventions such as drug-treatment can disadvantage occupational functioning in new patients suffering from schizophrenia with a pre-treatment duration of illness of less than a year. This finding has face validity but unfortunately the paper by Johnstone *et al* (*Journal*, August 1990, **157**, 182–189) indicates the strength of this and all other associations only by providing a *P* value. I find this a great pity, and surprising, in a paper which addresses associations and has performed a logistic regression analysis (which yields measures of association). All a *P* value shows is the probability that an association could have been found by chance; it does not offer information about the strength of the association. If numbers are large, relatively low associations will be significant. The relevant statistical indicators are the correlations, and their confidence intervals between reported predictors and outcome, informing us of the amount of variation in outcome that can be explained by these predictors. I hope that these figures will be forthcoming, strengthening the importance of this study.

I was also unclear about the reason for the classification of all the unemployed as poor outcome, especially since the unemployed category contributed 88% of patients in the poor-outcome group, without any clarification as to whether these patients had always been unemployed, had become unemployed as a consequence of the illness before admission, or became unemployed after admission. An earlier paper reporting on the same patients (Johnstone *et al*, 1986) shows that 67 of the 253 patients (26%) were unemployed on admission. Assuming this group remained unemployed, they would either form 67% of good outcome patients (being unchanged) or 50% of the poor outcome group (being unemployed). Either decision is debatable and requires a justification. Possibly a refinement of outcome criteria is indicated, since such a homogeneous classification of unemployed patients may explain some of the significant correlations, and may have led to important but potentially misleading conclusions. I am looking forward to a clarification on this issue.

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JOHNSTONE, E. C., CROW, T. J., JOHNSON, A. L., *et al* (1986) The Northwick Park study of first episodes of schizophrenia: 1. presentation of the illness and problems relating to admission. *British Journal of Psychiatry*, **148**, 115–120.

AUTHORS' REPLY: We are grateful to Dr Muijen for his interest in our work and are sorry that he has found some aspects less than clear.

We are aware of the difficulties of statistical assessment in data like this, where a large number of variables are being assessed. We took this into account in our methods of calculation and mention the need for caution in the interpretation of data of this kind in the text. There are different views about the best means of dealing with this kind of data set, and it may help Dr Muijen to know that the analysis in the paper is a compromise between our own initial ideas and those of two referees whose views were to some extent conflicting.

In the manuscript of the paper we initially included more information, but we were advised that the reader could be overwhelmed by the mass of data and that it would be better to highlight significant associations. From the point of view of most readers this is clearly good advice, although for those who are particularly interested in the data set it may be less than satisfactory. We would be pleased to provide interested colleagues with details of any particular aspect if they write to us directly.

We regret that we have expressed ourselves less than clearly with regard to the classification of patients' occupational outcome. Patients who were unemployed at follow-up were classed as unemployed even if they had also been unemployed at the time of the index admission. As may be seen from Table 5 of the paper, we did initially attempt a more refined classification of employment status, but the numbers who were employed in a higher status job were small and the numbers still in work but in a lower status not much greater. It is on the data in Table 5 that the result whereby good occupational outcome in patients with a relatively short pre-treatment duration was associated with the prescription of placebo medication during the follow-up period depends. All seven patients whose occupational status improved had a relatively short pre-treatment duration of illness. Six of them were prescribed placebo medication.

Dr Muijen indicates that he thinks we should not class patients as having a poor outcome because they are unemployed. There are many ways of looking at outcome in patients with illnesses which may be associated with long-term disability. For example, outcome in these patients has been considered in terms of relapse, death, in-patient days, judicial contact, ability to give child care and the rather non-specific concept of achievement. None of these measures, including employment status, is ideal and we understand from discussions with colleagues at the Maudsley Hospital that patients from their catchment areas are frequently unemployed and, even if they are reasonably well, are not likely to find work. This is not true of the areas in North-West London from which most of the patients in this study come. Many jobs are available, particularly for younger age groups. It is clear from the paper that many of the patients do work and it seems reasonable to say that at least in one sense the outcome in these patients has been better than that in the unemployed. Measures of outcome do not necessarily correlate. Perhaps the most disquieting finding of the study is the demonstration of better occupational outcome in patients with a short pre-treatment duration of illness who had been given placebo rather than active maintenance medication. In terms of relapse these patients did not do well but achieved their significantly better occupational outcome in the face of more relapses than similar patients prescribed active medication.

We hope that this letter provides the clarification that Dr Muijen seeks, but if there are any specific points he would like to discuss, he is most welcome to contact us.

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Gender-identity clinic patients

SIR: At a recent Journal Club meeting we discussed the paper by Burns *et al* (*Journal*, August 1990, **157**, 265–268), which proved to be interesting but contained some surprising incongruities in the tables of figures used. We note the following unexplained discrepancies.

The "DSM-positive" column of Table 1, the whole of Table 2 and the whole of Table 3 refer to the same population (DSM-positive transsexuals included in this study; $n = 77$). However, the breakdown of this group of people differed depending on which table you look at:

(a) In Tables 1 and 2 there are 20 members of the sample with a mean age of onset over 13, 54 under 13, and three whose age of onset is "unknown". In Table 3 there are now 20 with mean age of onset over 13, 53 under 13, and four "unknowns".

(b) In Tables 1 and 2 there are 27 members of the sample listed as heterosexual and 12 as "sexual orientation unknown". In Table 3, 26 are listed as heterosexual and 13 are "unknown".

(c) In Table 1 only one DSM-positive transsexual displayed sexual arousal with cross-dressing and 69 did not. In Table 2, seven DSM-positive transsexuals displayed sexual arousal with cross-dressing and 67 did not. In Table 3, 10 DSM-positive transsexuals displayed sexual arousal with cross-dressing and 63 did not. The remainder of the 77 people (7, 3 and 4 respectively) were listed as "unknown" in each category.

(d) In Tables 1 and 3, 24 DSM-positive transsexuals were referred for surgery and 53 were not. In Table 2, 24 were referred for surgery, 49 were not and four were "unknown".

We would be interested to hear the authors' response to these seeming inconsistencies.

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Authors' reply: We are grateful to our colleagues at Chase Farm Hospital for pointing out the discrepancies in the Tables of our recent paper, and are flattered that the paper was chosen for such close scrutiny in what sounds like a stimulating Journal Club.

To answer the points:

(a) and (b) This was due to the erroneous transposition of one case (a heterosexual in the onset < 13 group) from Tables 1 and 2 to the "unknown" category in Table 3.

(c) A proof error occurred in Table 2 and the column under core positive with regard to sexual arousal for cross-dressing should read 3, 30, 2 and not 0, 33, 2. After this correction, Tables 2 and 3 then agree in that there were ten subjects with sexual arousal. The discrepancy between these tables and Table 1 is due to the definition used which was slightly different when assessing the DSM–III criteria and the presence of core transsexualism – in the former it was defined in terms of arousal with cross-dressing (a narrower definition) whereby in the latter, a slightly wider definition was used to capture the sense of a total absence of sexual arousal in any aspect of the adoption of the cross-gender role.

(d) This was due to the addition of an "unknown" category to the "referral for surgery" in Table 2, whereas in Tables 1 and 3 these were included in the "not referred" group. To the best of our knowledge, these individuals were not referred for surgery.

While thanking Dr de Taranto and colleagues for bringing this to our attention, we feel these changes do not alter the main results or implications of our study.

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Musical and verbal hallucinations

Sir: Berrios (*Journal*, February 1990, **156**, 188–194) produced a useful literature review and statistical survey of cases of musical hallucinations. However, he does not seem to have read my related review of unilateral auditory hallucinations (Gordon, 1987) nor even my addendum in this journal (Gordon, 1988) drawing attention to it. Hence many interesting points were left unexplored and my conclusions were unchecked. Furthermore, it is now being cited as a 'definitive review' (Shapiro *et al*, 1991). To take some specific points:

Despite reporting personal cases with both musical and verbal hallucinations, Dr Berrios confined his review to musical ones only. Cases in the literature with otopathic auditory hallucinations cannot be clinically differentiated by type (i.e. music, words or elaborated tinnitus). Musical ones are admittedly quite striking given the specific and stirring quality of the evoked music. Indeed, it may not be coincidental that so many great composers had ear disease (Beethoven, Smetana, Schumann, etc). Nevertheless, most attention should be directed to non-musical auditory hallucinations, given their prominence in psychosis.

My references contained cases of musical hallucinations unused by Dr Berrios. There are undoubtedly others not cited by either of us.

I reported interesting relations between the laterality of the ear disease and hallucinations, but did not pursue this. Dr Berrios missed the chance to check this and did not even mention the subjective source of the hallucinations in any of his six new case vignettes.

My claim that hallucinations were more closely related to middle rather than inner ear deafness and to serous rather than purulent otitis was not assessed.

Dr Berrios made no distinction between unilateral and bilateral hallucinations. In medicine, causes of unilateral and bilateral diseases are often quite different. Focusing, as I did, on unilateral hallucinations simplifies correlation with ear or brain disease. Although I do not doubt that ear disease can produce bilateral hallucinations, it is very difficult to show this, even if true, from published reports.

He does not discuss the crucial question of whether ear disease without central disinhibition or neurological or psychiatric disease is a sufficient cause of auditory hallucinations. If so, concomitant brain disease may be a red herring. Dr Berrios claims a link between right hemisphere lesions and musical hallucinations, unsupported in recent well studied cases (Cambier *et al*, 1987; Shapiro *et al*, 1991). This makes it even more unfortunate that he had no comparable matching group of non-psychotic patients with verbal hallucinations linkable to left hemisphere lesions.

Dr Berrios ignores the literature on brainstem auditory hallucinosis. Cambier *et al* (1987) reported four such cases with typical religious/patriotic/music-hall themes, attributed to auditory deafferentation. In fact, the site of lesion was ambiguous, although all had brainstem lesions and none cortical ones. All were bilaterally deaf and auditory nerve lesions could not be excluded audiologically; the brainstem neurological symptoms resolved but not the deafness. A further case with an apparently pure brainstem lesion had primitive auditory hallucinations during one night of insomnia.

I conclude that Dr Berrios's review (and mine for that matter) were both incomplete, and it is unfortunate, but predictable, that his review is now taken as the last word up to 1989 on musical and related hallucinations.

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Failure to convulse with ECT

Sir: Failure to convulse with electroconvulsive therapy (ECT) has been estimated to occur on up to 21% of occasions that the electrical stimulus is administered (Pettinati & Nilsen, 1985). The topic has received much attention in recent years in the *British Journal of Psychiatry* (e.g. *Journal*, January 1988, **152**, 134–136; *Journal*, April 1988, **152**, 571; *Journal*, May 1988, **152**, 712–713). Following my own correspondence (*Journal*, May 1990, **156**, 747–748) I have been made aware of the Royal College's recommendations (Freeman *et al*, 1989) concerning what should be done if there is no observable seizure during ECT. While welcoming these guidelines, it is interesting to contrast them with those of the American Psychiatric Association (1990). The two regimens differ, for example, in:

(a) the number of restimulations that can be applied
(b) the requirement that a designated time elapse between restimulations
(c) the magnitude of the parameters of the repeat stimuli.

Although unsafe practice cannot be inferred from diverse practice, there clearly remains a need for a more uniform protocol, validated by empirical data. It is sobering to recall that when ECT was first attempted, in mid-April 1938, the initial stimulus of 70 volts for 0.2 seconds was unintentionally subconvulsive. Cerletti remembered (Cerletti, 1950) that a voluble discussion then broke out among the spectators, who included Bini, Longhi, Accornero, Kalinowski and Fleischer. Most objected to a further shock. The patient himself protested: "Non una seconda! Mortifera!" (Not another! It will kill me!). With some trepidation Cerletti decided to administer another stimulus of 110 volts for 0.5 seconds and the patient convulsed. It is a sad reflection on our discipline and, in this era of quality assurance, perhaps unsatisfactory that the protocols that have been devised to allay Cerletti's trepidation continue to lack empirical support and are often conflicting.

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Anorexia nervosa in the elderly

Sir: I read the report of "anorexia nervosa" in a 73-year-old woman by Cosford & Arnold (*Journal*, February 1991, **158**, 286–287) with interest. This lady suffered her (first?) episode of marked weight loss, food avoidance (why?), fear of weight gain and amenorrhoea after a loss at the age of 23 years. She received an unstated treatment over nine months as an in-patient. Fifty years later she "suffered a relapse, with severe weight loss, a distorted body image and a fear of becoming fat". This time she was put on a strict diet and was discharged after five months. This makes 14 months in-patient treatment. Is there an alternative explanation? Was it an atypical affective disorder. Did the passage of months (*and* the affective episode) provide the 'cure'?

Bernstein (1972) described the successful treatment of a 94-year-old woman with "anorexia nervosa" with electroconvulsive therapy. The reader was left wondering why this lady with a delusion that her food was being poisoned was not diagnosed as chronic paranoid schizophrenia.

Surely it would be wiser to apply the terms atypical anorexia nervosa or anorexia nervosa-like to such cases (Arya, *Journal*, February 1991, **158**, 285–286) until more is known about their (psycho-) pathogenesis.

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Chronic fatigue syndrome

SIR: I read with interest the article by Hickie *et al* (*Journal*, April 1990, **156**, 534–540) about the chronic fatigue syndrome (CFS). It inspires a few reflections concerning the criteria and the study, and concerning the existence of the CFS itself.

Their criteria are of two orders: psychological and immuno-infectious. It risks associating two different types of patients: some with post-infectious syndrome and some with psychological problems. Fatigue is one of the most common symptoms in medicine (Adams, 1980; Bugard, 1989). Patients with 'fatigue', 'concentration/memory impairment' and occasional 'lymphadenopathy' may have diagnosis of CFS. What is the frequency of lymphadenopathy in the general population? What do we know about relations between fatigue, depression and immunological deficit? Is not chronic fatigue usual in infectious diseases and after?

What is the interest of a control group "selected from the in-patient and out-patient psychiatric services"? Why not from medical units? Do the authors suppose that the difference between the group of patients with CFS and the control group is necessarily non-psychiatric?

The authors find 29 cases of depression among 48 patients with CFS but they say CFS is different from depression and near medical pathology. Is CFS a medical equivalent of depression (Rodin & Voshart, 1986)? We might test this hypothesis by using antidepressant drugs in CFS or looking for the presence of the same biological disorders both in CFS and depression. The GHQ and Zung scores are elevated as with medical patients. Severe depressive disorders are rare in CFS. However, this quantitative result does not exclude the association of depression and CFS.

The authors make the interesting hypothesis of clinical similarities between CFS and depression. They show it to be false, but CFS could be culturally differentiated depression with overmedicalisation. The patients with CFS had the "conviction that they are physically ill" and "they held this belief and rejected psychological interpretations". According to Balint (1972), a medical rather than a psychological diagnosis is favoured, which could increase diagnosis of CFS and reduce those of depression or hysteria and other equivalent diagnoses in DSM–III–R (American Psychiatric Association, 1987). As stated by the authors, the patients with CFS have a "reluctance to accept psychological interpretations of their somatic symptoms" and have a high score on the denial subscale. Criteria for CFS must be more stringent (e.g. previous history of documented infectious illness, no depression, presence or not of psychiatric symptoms, etc).

Further studies are required to remove the confusion between CFS and depression. They should analyse the psychological context at the beginning of CFS and its psychological evolution. They will define whether fatigue is a result of, or only increased by, infectious disease, whether depression is cause or consequence, and whether CFS is a morbid entity or the somatic expression of a psychological disorder.

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Family intervention

SIR: There is a point raised by McCreadie *et al* (*Journal*, January 1991, **158**, 110-113) which merits special emphasis. The authors noted the disappointing results of family intervention when compared with previous accounts (see, for example, Smith & Birchwood, *Journal*, May 1990, **156**, 654–660). The authors, in their discussions of this discrepancy, point out that the Nithsdale family treatments were given by "experienced practitioners, but who did not have special skills in family intervention in schizophrenia". This point is crucial if future reports along these lines are not to cast doubt on the established value of specialised family intervention.

Anyone who has worked in a team which specialises in family interventions with schizophrenia will be able to confirm that the work is both distinctive and sophisticated. They will also be able to confirm that it is not generally recognised, often even by knowledgeable and experienced colleagues, that successful family intervention requires specific training, preferably with a specialised team.

In this sense "The application of the results in a routine way to the work of the busy clinical team..." (Kuipers & Bebbington, 1988) is no trivial enterprise – not that these authors imply it should be.

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Uraemia and mania

SIR: I wish to comment on Thomas & Neale's case report (*Journal*, January 1991, **158**, 119–121). The authors describe a case of mania "secondary to advanced uraemia" caused by polycystic disease of the kidneys in a 62-year-old woman. I question that mania was secondary to advanced uraemia, for the following reason. Their case had chronic renal failure. Nine days after the beginning of haemodialysis she became manic. At that time urea had fallen. As mania appeared after haemodialysis, when urea was falling, it seems more likely to me that haemodialysis precipitated the episode in a predisposed individual.

I have recently described a patient with chronic renal failure who developed mania following abrupt nicotine withdrawal (Benazzi, 1989). Mania worsened when haemodialysis was started for the first time.

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The social networks of long-term patients

SIR: The finding of the TAPS project (*Journal*, December 1990, **157**, 842–852) that long-stay patients' responses to the Social Network Schedule (SNS) corresponded with observational data is reassuring. We have been using different versions of the Goodmayes Network Analysis Questionnaire (GNAQ) which is similar to, and I understand influenced the development since the early 1980s of, the SNS. As with the SNS, about two-thirds of patients on long-stay wards have been able to respond and the average size of networks has been similar; but individual variation is wide with some very large, as well as very small, networks.

The general picture from two surveys is of networks containing a substantial number – but rarely all and frequently not a majority – of the residents on the same ward as the respondent, together with an important proportion of patients from other wards who were particularly likely to be seen as friends or confidants. Some contacts had clearly been maintained for, or revived after, very long periods, despite being undermined throughout the years by moves without consideration of networks. Relationships with staff both on and off the ward were very important but in contrast there were few contacts with people outside hospital apart from relatives. It is an irrecoverable loss that relationships between patients within mental hospitals, which must have been a major factor in ameliorating the institutional experience, were not systematically explored much earlier. As a result they were undervalued as the deinstitutionalisation movement developed and no account was taken of them in earlier studies of patients' attitudes to discharge (Abrahamson *et al*, 1989).

At Goodmayes Hospital it has proved both illuminating and useful to seek to maintain existing networks and re-establish old ones, as well as fostering new contacts, during preparation for resettlement. These remain important after discharge, since merely placing long-stay patients out of hospital does not ensure a wide range of contacts 'in the community'; former relationships are the main, and often the only, feature of hospital life to be missed. Our experience of group homes over the past 19 years supports the TAPS concern that despite their other benefits the small, relatively intense networks they foster may be unsuitable for some patients.

As suggested, social clubs may compensate, and an encouraging range of relationships has developed within and around an evening club established in 1987 in Newham, in conjunction with a group-orientated out-patients clinic which has itself expanded networks. Encouragement of social contacts across individual group homes and flats can also contribute. More basically, we have been impressed by the effect of adding to the range of medium-sized housing projects provided, which have been specifically designed to combine individual units and communal facilities. Their larger networks appear to be the more welcome because there are also greater opportunities to withdraw temporarily when needed: the difference in milieu seems to be to some extent analogous to that between extended and nuclear families. The first such project has been in operation since 1983 and recent schemes are catering very successfully for heterogeneous populations containing apparent isolates of the kind highlighted by the TAPS studies, including a number of profoundly deaf patients.

There has been a tendency to belittle arrangements that increase inter-patient contacts as promoting ghettos, but the evidence is that they encourage rather than inhibit the development of relationships in the wider community (Segal & Aviram, 1978) and it will be reprehensible if the institutional undervaluing of patients' social networks is repeated.

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Incestuous abuse in psychiatric patients

SIR: We read with great interest the article about incest in normal weight bulimic women by Lacey (*Journal*, September 1990, **157**, 399–403). We have also carried out research work on the prevalence of child sexual abuse in in-patients with neurotic and psychosomatic disorders. We think that our findings (Kinzl & Biebl, 1991) confirm and supplement Lacey's results.

Very serious and long-lasting child sexual abuse was found in female psychiatric in-patients with different psychopathologies and mental disorders (20% of the total sample). Self-damaging behaviours of different kinds and a tendency to "acting-out" proved to be the main symptoms of sexually abused patients; nearly all those patients showed multi-impulsive personality disorders (Lacey & Evans, 1986). Few of the patients surveyed were able to talk about child sexual abuse early in therapy and the majority were able to talk about it only after a long time of therapy; some will never talk about it. Because of the strong feelings of guilt and frequently marked suppression of the incestuous experiences the prerequisites for the disclosure are a lot of empathy, "real sympathy" (Ferenczi, 1949), and a reassuring therapist–patient relationship, as well as the therapist's readiness to talk about it and to believe what the patients say.

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Tolbutamide and fatal water intoxication

SIR: Peh *et al* (*Journal*, June 1990, **156**, 891–894) present an instructive case reminding us of the serious risks of unrecognised hyponatraemia in psychiatric patients ("psychogenic polydipsia"), but fail to note a possible significant contributing factor towards their reported patient's unfortunate demise.

The individual in question was first recognised to be hyponatraemic some time after being started on a regimen which included tolbutamide (500 mg t.d.s.). As with the related sulphonylurea chlorpropamide, tolbutamide has an antidiuretic action in normal adults and has been associated with dilutional hyponatraemia in several published case reports (Hagen & Frawley, 1970; Gossain *et al*, 1976; Darlow, 1977; Lichtenberg & Abraira, 1978; Kadowaki *et al*, 1983). In one of these cases, an individual receiving the same modest dose of tolbutamide (500 mg/day) presented with serious hyponatraemia, twice replicated on rechallenge (Lichtenberg & Abraira, 1978). Upjohn, the manufacturer of the Orinase brand of tolbutamide, has received reports of another nine cases (personal communication). A retrospective review of 108 patients treated with tolbutamide for an average of 6.6 years found five (4.6%) had a recorded serum sodium less than or equal to 134 mmol/l, including one (0.9%) with a value of less than or equal to 129 mmol/l, and a complication rate less than that of a comparison group receiving the more common offender, chlorpropamide, but greater than that of a group receiving glibenclamide (Kadowaki *et al*, 1983).

Psychogenic polydipsia (an ill-advised term; the presumption of a psychogenic aetiology is far from established) has appropriately received attention as a poorly understood syndrome, but several agents are well established contributing factors in many cases, and deserve recognition. The use of nicotine, thiazide diuretics and carbamazepine are most commonly implicated, but we should not forget the occasional patient who may be treated with chlorpropamide, tolbutamide, clofibrate, cyclophosphamide or vincristine.

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Tardive oculogyric crisis and obsessional thoughts

Sir: Before the introduction of neuroleptics, the most common cause of oculogyric crises (OGC) was post-encephalitic Parkinsonism. In these patients, OGC was found to be commonly associated with a variety of transient mood and thought disturbances, including obsessional thinking (Stern, 1927). Although patients suffering from drug-induced OGC are known to secondarily become very anxious (Dorevitch, 1984), an association with obsessional thinking and compulsions has been reported in only one case (Leigh *et al*, 1987). The case described below is significant for two reasons: the patient had a late-onset and recurrent OGC while on neuroleptics, and the episodes of eye deviation were frequently associated with obsessional thoughts.

Case report. A 47-year-old woman was first treated for schizophrenic illness 20 years ago with trifluoperazine for six months with gradual and complete recovery of her delusions and auditory hallucinations. Obsessive–compulsive symptoms were not noted as part of her illness, nor were marked obsessional traits a feature of her pre-morbid personality. Following a relapse two years later, she was again treated with trifluoperazine for 2 months, and then maintained on depot fluphenazine decanoate until the present, with doses varying from 12.5 mg every four weeks to 25 mg per week.

About two months after starting fluphenazine decanoate, she developed recurrent episodes of OGC which failed to respond to benztropine (12 mg/day) and improved markedly with procyclidine (20 mg/day), on which she has been maintained ever since, with 2–3 episodes of OGC per week. The episodes occur most frequently in the afternoon but have no reported relationship to fatigue, psychological stress or day of injection.

The description of the OGC provided by the patient was fairly stereotyped. One episode was observed by the author when she agreed to stop her procyclidine for a day. No precipitant was obvious. She became anxious and markedly distressed, and her eyes deviated upward and slightly to the right; the frontalis and nuchal muscles contracted, with retroflexion of the neck. There was no strabismus or skew deviation and she could move her eyes in the upper field of vision. During the episode, she had repetitive and intrusive thoughts about her children: "Are they my children?" and "What would it be like without children?". These thoughts were unwanted, resisted unsuccessfully and were not elaborated into delusions. Twenty minutes after taking 5 mg procyclidine orally, the OGC ceased, and with it her repetitive thoughts. She reported having had obsessional thoughts during many, but not all, episodes of OGC. The main themes had been: counting repeatedly (e.g. numbers from 1 to 10, steps in her office, number of lights in the house, totals of purchases in the shop), romantic thoughts involving her with various men, and her children. No obsessions or compulsions were present unrelated to the OGC. If untreated, the OGC usually lasted for many hours, with the longest duration having been 14 hours. She was unable to abort the attacks. Additional relevant observations were the presence of tardive akathisia and mild tardive dyskinesia.

That this striking association between drug-induced OGC and obsessions has rarely been reported may be because it is seen only in the tardive OGC syndrome which itself is probably rare (Fitzgerald & Jankovic, 1989). This association permits speculation on the morphophysiological basis of the two disorders. For example, while dopamine has been the focus of attention in OGC, and serotonin in obsessions, our case suggests that the situation is likely to be far more complex.

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Drug-induced koro in a non-Chinese man

SIR: Anderson (*Journal*, July 1990, **157**, 142–144) describes a case of koro in an elderly non-Chinese patient with post-stroke depression. Koro is a syndrome characterised by a belief that the penis is shrinking and will eventually disappear into the abdomen and result in death. In its classic form, koro has been described predominantly in Chinese patients in South-East Asia and has been considered to be a culture-bound syndrome of depersonalisation (Yap, 1965). In non-Chinese patients a small number of sporadic cases have been described and reviewed (Berrios & Morley, 1984). It was found that most patients have another primary psychiatric disturbance, with the koro complex grafted onto existing symptoms. The majority of non-Chinese cases in the literature are aged under 65 years. A further case of koro in an elderly Englishman is described.

Case report. A 69-year-old married, retired security officer was referred from a surgical ward following his admission with urethral trauma. He had inserted a knitting needle into his urethra in the belief that his penis was shrinking into his abdomen, thus causing obstruction to urine flow.

Born and brought up in Nottinghamshire, he had no known family history of psychiatric illness. During the war he served with the Army in Northern Europe and afterwards spent two years in India. He was married with two children. There was no history of sexual difficulties, or drug or alcohol abuse. He had no previous psychiatric contact.

About six months before presentation, idiopathic Parkinson's disease was diagnosed and L-dopa therapy initiated. Two months before presentation he developed a depressed mood with transient auditory and visual hallucinations. Gradually he developed a firm belief that his penis was shrinking into his abdomen. Several days before admission he reported a poor urinary stream and was convinced that the penile shrinkage was mechanically blocking his urine flow. He decided he must act before his urine flow stopped completely and inserted a knitting needle into his urethra.

On assessment, he was agitated but alert and fully orientated. He was preoccupied with the firm conviction that his penis was shrinking into the abdomen. There was no associated fear of death. He described visual hallucinations and illusions (e.g. swimming eels in the bath), as well as a depressed mood with sleep and appetite disturbance. There was no evidence of cognitive impairment, and results of physical investigations were within normal limits.

Anti-Parkinsonian medication was withdrawn and he was treated with small doses of neuroleptics. His mental state gradually improved and the delusion of genital shrinkage subsided three days later. His Parkinsonian symptoms necessitated a limited reintroduction of L-dopa therapy which resulted in occasional episodes of visual hallucinations during which insight was retained. He had no recurrence of his delusion. His urinary symptoms improved after urological investigations, which revealed no evidence of prostatic hypertrophy.

This case of koro symptom complex in the context of an organic psychosis caused by L-dopa therapy adds to the small number of patients with koro in the context of organic disorder which are described in the literature. Descriptions of koro in elderly patients are rare. As with Anderson's patient, this patient also had a strong affective component in his presentation. Interestingly, in both patients urinary symptoms were prominent in presentation. Anderson's patient presented with acute retention of urine subsequent to his belief that penile shrinkage would lead to outflow obstruction. In both patients, therefore, delusions of penile shrinkage were followed by the idea that the passage of urine would become impossible once the shrinkage was complete. This idea is surprisingly rarely encountered in other cases described in the literature and may reflect a pathoplastic effect of age on the koro symptom complex.

Koro in non-Chinese patients is associated with a range of psychiatric conditions. Anderson points out the need for vigilance in order not to miss or misdiagnose the underlying disorder. In addition to awareness of any concurrent psychiatric symptoms, exploration into the nature of the fear associated with genital retraction may provide an important insight into the psychopathology of the patient.

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A HUNDRED YEARS AGO

The Nursing of the Insane

The Council of the Medico-Psychological Association are pressing forward their scheme for organising a system of practical instruction for nurses and attendants in asylums, to be followed by examination and the granting of special certificates to those who are successful in passing the requisite standard. Already a goodly number of candidates have entered, and encouraging reports are being received of the satisfactory progress the work is making in all parts of the kingdom. In this connection it is worthy of note that the London County Council have granted permission to Dr Ewart, of the Colney Hatch Asylum, to deliver a course of lectures, under the rules of the St John Ambulance Association, at this asylum, and we trust that Dr Ewart, who is himself a member of the Medico-Psychological Association, will supplement this useful work by endeavouring to encourage the nurses and attendants to proceed to acquirement of the certificate of the Association, which will enable them to become qualified as specially trained in the nursing and care of the insane. This has already been done with much success at the City of London and one or two other asylums, and we are glad to think that there is an increased activity in this direction throughout the asylums of the country generally.

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British Medical Journal, 9 May 1891, 1032.

Researched by Henry Rollin, Emeritus Consultant Psychiatrist, Horton Hospital, Surrey.

British Journal of Psychiatry (1991), **158**, 723–725

Reading About . . .

Group Psychotherapy

Since Bloch (1981) last wrote about the group psychotherapies for this journal, there have been significant developments in practice and in the available literature. There is now a wider range of introductory texts, and a few works have extended the theory of group dynamics and the therapeutic action of groups. There is evidence of a growing awareness of the applications of group psychotherapy in the treatment of a range of patients.

For the beginner who is looking for a short introduction, there are useful chapters in three well known books. Brown & Pedder's (1979) brief section on psychodynamic group psychotherapy is set in a clear text which outlines the general principles and practice of psychodynamic treatments. Whiteley & Gordon (1979) approach the subject from a more sociological perspective, offering a succinct summary of group dynamics and locating the small psychotherapy group in the wider setting of the therapeutic institution. Bloch's (1986) compact chapter addresses practical issues such as indications, selection and preparation of patients for group psychotherapy, and he illustrates typical developments in the life of a therapy group. I have explored the wider applications and implications of group processes in psychiatry (Hobbs, 1990).

Several books, both old and new, offer more extensive introductions to small-group psychotherapy. I was much influenced by Walton's (1971) slim text which, though now out of print, is still available in many libraries. This book offers the most concise outline of object relations psychology that I have ever read, and demonstrates its value in understanding group processes. Foulkes & Anthony's (1957) book, which has been reprinted, is still the most useful introduction to the group analytic perspective, giving a clear analysis of the nature of groups and the processes which occur within them.

Two recent books tackle the subject of group psychotherapy in contrasting styles. Wright's (1989) text was written for students undertaking an introductory course in psychodynamic group work, and offers perhaps the simplest introduction available today. He outlines the psychological development of the individual within the family and social network as a background from which to address the therapeutic properties of the group. Aveline & Dryden (1988) have edited a book which introduces the diverse range of group therapies practised in Britain today. There are clear chapters on analytic, interpersonal and cognitive behavioural group therapies, as well as valuable chapters on the therapeutic community, single-sex therapy groups and group therapy research.

Hinshelwood (1987), in his aptly titled *What Happens in Groups,* aims to establish a way of thinking about groups, communities and institutions in general, and therapeutic ones in particular. Whereas others have sought to understand the group in terms of individual psychodynamics, Hinshelwood applies his knowledge of groups to the individual. Kernberg (1980) has also written about the dynamic interaction between the individual and the group, and I have found particularly useful his succinct description of the impact on institutions of the leader's personality.

It is also important for today's student of group psychotherapy to be able to trace the emergence and development of the theory and principles which underlie current practice. Although Freud did not address the therapeutic application of the group, he did make astute observations of group dynamics in his *Group Psychology and the Analysis of the Ego* (1921). The development of group psychotherapy in Britain was stimulated initially by the work of a small number of psychoanalysts during World War II. Bion's interest in the therapeutic application of groups was short-lived but his observations on the behaviour of groups of people remains salient today (Bion, 1961). Pines' (1985) compilation brings together some interesting observations on Bion's work and appraisals of the application of his theory of groups to understanding the dynamics of organisations and institutions. Foulkes (1948, 1964) derived his simple but comprehensive ideas from his work in therapeutic groups, and his books outline the historical and theoretical basis of group analysis. The continued evolution of this approach has been traced in another compilation edited by Pines (1983).

There is really no such thing as a manual of group psychotherapy, but there are books which are very useful practically to the group psychotherapist.

Yalom's *The Theory and Practice of Group Psychotherapy* (1985) has long been a valued reference for group therapists. It is extraordinarily comprehensive and offers useful practical advice to guide the therapist in many tricky situations. Yalom draws extensively on his own clinical experience and on accumulated findings from empirical research. The book forms an excellent summary of interpersonal group psychotherapy, a model derived from existential and humanistic traditions.

What Yalom has done for interpersonal group psychotherapy, Rutan & Stone (1984) have done for psychodynamic group psychotherapy. They address many of the technical aspects of group psychotherapy from a clear-cut psychodynamic perspective, and achieve a wonderfully lucid digest of the subject which offers wisdom without being prescriptive.

In very different style, Whitaker (1985) has written a book for those who are planning or conducting psychotherapy groups. She sets out the necessary decisions and tasks for the group therapist in a clear and straightforward way, addressing many practical issues, questioning assumptions and stimulating thought about the processes entailed in selecting, establishing and conducting treatment groups.

Interest in group psychotherapy has progressed from the classic out-patient model, which is the subject matter of most of the books referred to so far, to the therapeutic application of groups for specific client populations.

Yalom (1983) and Rice & Rutan (1987) have written practically orientated texts about small-group psychotherapy for in-patients; from interpersonal and psychodynamic perspectives respectively. Both books examine the nature and impact of the in-patient setting on the group, and the modifications of technique required for group psychotherapy with acutely disturbed patients. In-patient group psychotherapy is often an adjunct to other methods of treatment, and flexibility in therapeutic style is recommended. Both books suggest provision of a hierarchy of treatment groups to cater for patients with different levels of psychological functioning, through which each patient can progress as he/she recovers from the illness which precipitated admission to hospital.

Over the past few years, a number of books have been published in North America which explore the applications of group psychotherapy in the treatment of specific populations such as alcoholics, drug abusers and elderly psychiatric patients. One of the few which is readily available in Britain is Ganzarain & Buchele's (1988) book about the group treatment of adult victims of childhood sexual abuse. They describe long-term analytic group psychotherapy with women victims, most of whom are highly disturbed and prone to dissociation, and impulsive and self-destructive actions. They offer observations on transference, countertransference and other dynamic processes which are valuable for understanding work with this client population in any setting.

Psychotherapy groups are complex, and empirical research is problematic. The pace of outcome research is slow, but considerable efforts have been devoted to the study of group process, and particularly to the therapeutic action of groups. Bloch & Crouch's (1985) summary of the empirical research into 'therapeutic factors' is detailed and comprehensive.

Several authors have sought to extend our theoretical understanding of psychodynamic therapy groups (e.g. Agazarian & Peters, 1981; Anzieu, 1984). My interest was stimulated particularly by the scholarly work of Ashbach & Schermer (1987) who attempt the development of a psychology of the 'group-as-group' through an integration of object relations, self, and group analytic psychologies. Their concept embodies three fundamental premises. Firstly, the individual and the group both emerge from a primal unity through the creation of a boundary which distinguishes one from the other. Secondly, the group and the individual are but two sides of the same coin, intrapsychic and group processes being complementary manifestations of a field of psychological action which embodies both. Thirdly, they suggest that intrapsychic, interactive and group-as-group processes are inter-related dynamic systems within the group, each of which functions as a container of experience. Within the space of the group, previously unbearable mental experience can be transformed into safe and tolerable interactions through which the private self can emerge into a harmonious social identity. There is enough food for thought and development in this one book to keep us going for the next decade.

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Book Reviews

Editor: Sidney Crown

Continuities of Deprivation? The Newcastle 1000 Family Study. By I. Kolvin, F. J. W. Miller, D. McL. Scott, S. R. M. Gatzanis and M. Fleeting. London: Gower Publishing. 1990. 408 pp. £38.50.

This book is the final volume in the "Deprivation and disadvantage" series. Following a provocative ministerial speech in June 1972 from Sir Keith Joseph, the then Secretary of State for Social Services, regarding the circumstances which prevent people from developing their full potential, a wide variety of professionals were prompted into initiating many studies to look at the concept and process of 'deprivation'. This text reports on a prospective longitudinal study of 1000 families in the Newcastle area.

This particular study was based on the concept that the total environment of a child influences all aspects of his or her development and functioning, that is, their physical, social, emotional and intellectual capabilities. If an optimal family environment was lacking then this may ultimately affect the child's development in any one of the four mentioned spheres, which if not recognised and remedied may persist into adult life. Not only may the suboptimal functioning continue into adult life, but it may then affect the next generation of children who will then, in their turn, also receive inadequate care. It is these aspects of the processes involved in such proposed 'cycles of deprivation' that this study has attempted to elucidate.

The book starts by describing the origins and methodology of the study. Indeed, it is particularly frank in drawing attention to its own methodological problems regarding the type of data collected and the particular concepts of deprivation that the study utilised. There then follow five main sections each concerned with the particular area of the study. Firstly, there is an extremely detailed account of the demographic factors concerning the families of origin, the so-called 'red spots'. This is then pursued in the subsequent section by looking at this cohort as children, in adulthood and in their choice of partners, and finally at the children of these people. The book then turns to consider and provide exhaustive data on the changes that had occurred within generations and also across generations.

Having presented this material the statistical analysis and approach of this data is considered in some depth. A further section attempts to look at the association of deprivation and offending behaviour, and our current ability to predict criminality using this information.

The concluding chapters discuss at some length their findings and possible impact this has, not only on our understanding of the concept of deprivation, but also the possible importance of the certain factors in the maintenance of adverse sequelae. The conclusions are that whatever deprivation a child may experience, a fundamental family mechanism by which the child is affected is through inadequate physical and emotional care. The further mechanism they believe to be of fundamental importance concerns that of a concept of 'educational handicap'. Although the precise processes are not fully apparent it is an important predictor of low occupational rating, unemployment and poor mothering ability. In fact, it is the multiple, rather than the single, deprivations that appear to have such widespread and damaging effects.

This volume contains a wealth of detailed information. Anyone who is faced with considering the mechanisms of the persistence of adverse experiences in one generation to the next will find this very full delineation and discussion of the Newcastle 1000 study invaluable.

Marian Perkins, *Senior Registrar in Child and Adolescent Psychiatry, Maudsley Hospital, London*

Psychologists and Child Sexual Abuse. By The British Psychological Society: Report of a working party comprising Neil Frude, Anne Peake, Jean Sambrooks, Peter Stratton and Chris Cullen. Leicester: The British Psychological Society. 1990. 16 pp. £5.00.

It is difficult to see for whom this curious little pamphlet is intended. Its 16 pages, in huge print, and including a small bibliography, appear to be an exhortation to other professions to recognise the importance of psychology – or psychologists: the two are here confused.

It seems to me unlikely that other workers in this field are unaware that psychology is involved and this report contains very few research findings. On the other hand, if it is psychologists who are being marketed here, there are problems in the areas of both assessment and treatment. It is suggested that psychologists have "special assessment skills", which would seem to imply face-toace contact between psychologists and putative victims (here called "survivors"). However, given the emerging scale of the problem and the available number of clinical psychologists, this seems somewhat unrealistic. (I recently visited one district where the psychology service promised to a Community Mental Health Support Group was withdrawn completely, having been overwhelmed by the demand for help!). We are not told what the "special assessment skills" are or whether they could be taught to non-psychologists.

In relation to treatment, it is suggested that psychologists "work through other staff" by being "heavily involved in their training". This would seem more realistic, but realism reaches extraordinary depths, bordering on either cynicism or narcissism, when the authors state that "The *goals* (my emphasis) of intervention will depend ... to some extent, on the kind of therapy offered by the particular psychologist".

The authors also suggest that psychologists may have a role in 'supporting' those who are involved in the field of sexual abuse. In addition"we may be uniquely well placed to contribute to advice on structures and procedures which would optimise interprofessional co-operation".

As for prevention, the authors acknowledge that "there is, so far, an inadequate research base for programmes of prevention". Are psychologists substantially contributing to this research? What does it mean when the authors tell us that the BPS is "supporting" it?

CHARMIAN BOLLINGER, *Chartered Clinical Psychologist, Kneesworth House Hospital, London*

Handbook of Clinical Assessment of Children and Adolescents, Vols I & II. Edited by CLARICE J. KESTENBAUM and DANIEL T. WILLIAMS. New York & London: New York University Press. 1988. 1170 pp.

The appearance of a new textbook in child and adolescent psychiatry has become a rarer event than it used to be, but the publication of a new American two-volume text is bound to be of great interest. The contributors to this multi-authored textbook are entirely drawn from psychiatrists and psychologists working in the USA, indeed they mainly come from prestigious centres in and around New York. The title of the book is misleading in that there is a large section on treatment approaches, and most of the chapters deal with management as well as assessment.

As might be expected, the structure of the book is heavily yoked to the DSM–III classification. In the introduction the editors stress the change in American child psychiatry from an anecdotal, discursive approach based exclusively on a psychoanalytic model, to an approach much more strongly linked to empirical findings. This change is largely reflected in the contents, although there are exceptions. In the 1990s, it is difficult to continue to recommend the use of the Rorschach, even as a projective test, and the discussion of the psychosexual development of the pre-pubertal child is firmly free of any constraints provided by the empirical literature.

There are, however, many excellent chapters, too numerous to mention individually. I learned most from the chapters on pre-school language assessment, pervasive developmental disorders, and drug and alcohol problems. The increasing reliance that American clinicians place on questionnaires and structured interviews in making their assessments is noteworthy. For example, in the highly technically competent account of the assessment of anxiety disorders, there is a detailed description of the scales available for use, but no mention at all of the clinical skills that can be deployed to assess the functional disability produced by anxiety states, or those that can be used to link a child's anxiety with those of other members of the family, especially the parents.

These reservations apart, this two-volume textbook contains a great deal of value. It will probably not be the first choice of textbook for psychiatric libraries or specialist child and adolescent psychiatrists, but certainly should rank high among those currently available.

PHILIP GRAHAM, *Professor of Child Psychiatry, Institute of Child Health, London*

Annual Progress in Child Psychiatry and Child Development 1989. Edited by STELLA CHESS and MARGARET HERTZIG. New York: Brunner/Mazel. 1990. 576 pp. $50.00.

Yes, the editors of this annual review have done it again! They have successfully highlighted trends in original research and review over the previous year, as they have been doing annually for over two decades, thus ensuring that signal contributions of immediate topicality and lasting interest are brought to our attention and are not smothered by the profusion of journals and welter of publications in this and allied disciplines.

Ten themes have been selected, reflected in 33 papers which include studies of infancy, development, gender and race, special stress and coping, temperament, depression and suicide, clinical issues (covering AIDS), and adolescent issues. There are also papers covering the special issues of day care, and historical perspectives. The selection process cannot have been easy and called for breadth of vision allied to fine judgement regarding significant advances, rather than a blind dependence on distinguished departments or eminent names. The tour de force is the section on depression and suicide, with Klerman providing a focus on secular trends, Angold summarising developmental changes in psychopathology and biological manifestations, and a review of classificatory and diagnostic issues. Pfeffer's work gives an account of the course of suicidal behaviour and Shaffer and colleague provide a critical review of suicide prevention. Finally, Hoberman and Garfinkel address themselves to risk factors in adolescent suicide. Each of the other sections is almost as appealing, but to the psychiatric historian the real gem is the fifty year perspective by Chess of child and adolescent psychiatry, focusing on the issues that have impressed her, in association with the dramatic growth and coming of age of the speciality.

This series has never lost either its sense of direction, its freshness or its capacity for being an important source of key advances for the scientist and an update for the clinician. This rich and stimulating collection will have wide appeal which would be even wider if it were in a somewhat cheaper paperback form.

Hertzig has replaced Alexander Thomas as joint editor, but this is likely to represent continuity rather than ideological or stylistic change. As always, the book represents an old and welcome friend, this time in new clothes.

ISRAEL KOLVIN, *Professor of Child & Family Mental Health, The Royal Free Hospital, School of Medicine and the Tavistock Centre, London*

Children's Sexual Encounters with Adults. By C. K. LI, D. L. WEST and T. P. WOODHOUSE. London: Duckworth. 1990. 343 pp. £39.95.

Child Sexual Abuse in Northern Ireland. By THE RESEARCH TEAM. Northern Ireland: Greystone Books. 1990. 188 pp. £18.00.

"SHOULD SEX BEGIN AT 12?" headlines the Daily Telegraph newspaper (14 November 1990), in a report on the recent changes introduced by the Dutch Parliament concerning the age of consent to sexual relations. How do we define child sexual abuse, measure its incidence and assess the harm which might ensue?

In *Children's Sexual Encounters with Adults*, Li *et al* have produced a detailed work on adult–child sexual interaction. West and Woodhouse report on surveys of adult men who were asked to recall any sexual encounters as boys. Although limited by poor response rates, about one in five men reported boyhood experiences with older men or women, the majority being with men. Most incidents involved approaches, propositioning or touching and usually occurred in public places. Contacts with men were usually considered as uninteresting or irritating and most boys were capable of controlling the situation. Sexual contact with women, although less common, was usually viewed as pleasurable and was rarely harmful. Homosexual men in the survey were more likely to recall childhood contacts with adult men and were more likely to find such contact welcome or even sought after. There remained, nevertheless, a small proportion of all men who viewed such encounters as definitely aversive. As is the case for girls, boys from unhappy, broken or unsupervised homes were more vulnerable to sexual contact with adults. In contrast to women, however, far fewer men reported longer-term negative reactions.

After a detailed debate of previous work and the ethics of his own approach, Li reports in the second section of this book on the views and experiences of 20 men who admitted to sexual attraction to children. Subjects were enlisted from psychiatric clinics, a paedophile organisation and *Forum* magazine. Athough himself a psychologist, Li attempts to eschew all reductionist labelling of this behaviour in order to understand the feelings and motivations of such men through a detailed consideration of their testimonials.

Child Sexual Abuse in Northern Ireland is a report of a large-scale agency survey during 1987 of sexual abuse in Northern Ireland. It is a densely written report which concentrates on a careful assessment of the present problem. Child abuse is defined in a broad way ranging from sexual intercourse to "talking about sexual things in an erotic way". A child is considered as someone under the age of 17 years, the age of consent in Northern Ireland. Estimated incidence of reported cases over one year was calculated at 1.2 per 1000 children. Men were most commonly the abuser and girls the abused, although the incidence among younger boys was relatively high. Important associations with both the child and the abuser are described. Although the definition of abuse used might be open to criticism it is clear, and the incidence of various levels of abuse is also reported. The report ends with a recommendation that child care centres be established in each Health and Social Services Board of the country to deal with suspected cases, train workers and form links with other agencies.

What can be made of these two rather different approaches? Li *et al* challenge the prevailing assumption that child–adult sexual interaction is always harmful and that children are not capable of consent. I must admit that I found their view rather worrying, particularly as it was partly based on the views of paedophile men who would generally be expected to regard such sexual interaction as acceptable and harmless. Nevertheless, it was refreshing to read an intellectual challenge to our current views of the morality of sexuality as it is enshrined in law. As Li concludes: "the law is only a *practical* arrangement for the peaceful co-existence of individuals living in a community. It does not have, and should not be endowed with, a kind of absolute moral status." This book takes an unpopular stand and makes fascinating, if somewhat disturbing, reading. The Research Team in Northern Ireland take a more rigorous epidemiological approach based on more classical assumptions about what is sexual abuse. Should sex begin at 12? As Dutch law indicates, perhaps the answer is sometimes.

MICHAEL KING, *Senior Lecturer and Honorary Consultant, Royal Free Hospital School of Medicine, London*

Paediatric Epilepsy. Edited by Matti Sillanpää, Svein I. Johannessen, Gösta Blennow and Mogens Dam. Petersfield: Wrightson Biomedical Publishing. 1990. 377 pp. £45.00.

Considerable advance in the field of epilepsy has occurred in all age groups over the past 10 years, from the understanding of basic mechanisms to the use of newer imaging techniques. There are also signs that, as in other areas of medicine, molecular genetics will have an impact. In addition, newer anticonvulsants have been introduced. At this juncture, an update in paediatric epilepsy is clearly needed and this volume has much to offer, being conceived as a book rather than a collation of conference presentations. It consists of 37 chapters, some relatively short, but all succinct; the work of 41 contributors, nine from the USA, the remainder from Scandinavia. This point is neatly side-stepped in the preface by the statement that the book represents the view of Scandinavian experts. The preface also contains the disclaimer that the editors have not attempted conformity of opinion, which in fact adds to the value of the book.

It starts with five chapters on basics, epidemiology, pathology and genetics. Then follow 12 chapters on particular disorders ranging from neonatal seizures to benign partial epilepsy, and including sections on progressive conditions. There are four chapters on investigation including imaging methods and electroencephalogram (EEG). In the latter there could have been more emphasis on ambulatory monitoring and split-screen video presentation of patient and EEG, although this is mentioned elsewhere. Drug treatment and surgery are then covered. Then, there follow four chapters on what is called 'habilitation'. In spite of the oddness of the word it is quite clear that it concerns overall management as well as organisation of services. The book ends with chapters on discontinuation of anticonvulsants and prognosis. Each chapter is self-sufficient with its own good bibliography and there are appropriate illustrations including some in colour. A strong introduction and a concluding chapter would have been helpful, as would the grouping of the chapters into subsections.

The volume is well presented and comprehensive as well as up-to-date, and it is warmly welcomed.

D. F. Scott, *Consultant in Charge, Section of Neurological Sciences, The Royal London Hospital*

Depression in Mentally Retarded Children and Adults. Edited by Anton Dosen and Frank Menolascino. Leiden: Logon Publications. 1990. 362 pp. 95dfl/ $50.00.

This book joins a growing number of publications on psychiatric aspects of mental handicap. The Editors have attempted to draw together perspectives on depressive illness in mentally retarded people from several professional disciplines including child and adult psychiatry, educational psychology, child development and neurology, epidemiology, counselling and clinical chemistry. The result is a patchy, repetitive book which purports to be scientific but which ends up by being speculative in parts, uneven in quality and too often full of jargon.

There are some good contributions, however, particularly the chapters on clinical findings by Day, on biochemical studies by Ruedrich, on bipolar disorders by Sovner and on behavioural treatments by Benson. Some of the chapters on psychological and psychotherapeutic treatments such as relationship, milieu, developmental and symbolic-interactional therapy, are also intriguing. It would be more convincing, however, if these treatment methods were allowed to stand in their own right and were not pressed into service as treatments for depression. For example, it is very difficult to accept the diagnosis of major affective illness in a severely mentally retarded, non-verbal, non-mobile three-year-old child, on the clinical grounds stated, although there is no difficulty in accepting that the child improved with relationship therapy.

It is easy to be dismissive of this book, but that would be ungenerous. It is a genuine and well intentioned effort to convey the experience of depression from the mentally retarded individual's viewpoint, and some of the case vignettes are moving and authentic. It is client-centred and eminently caring and that alone makes it worthwhile. We are, however, now seeing a developing tendency to overdiagnose mental illness in mentally retarded people, and yet again, in a new context, to overmedicalise the subject. I doubt whether there is, in fact, enough quality research to justify a full length book on depression in mentally retarded people as yet.

Despite its scientific shortcomings, I think this book would be of interest to any professional involved in caring for mentally handicapped people in whom depression of mood and unhappiness may be a problem. I could not, however, recommend it as a suitable text for examination candidates.

Andrew H. Reid, *Consultant Psychiatrist, Dundee Psychiatric Services, Royal Dundee Liff Hospital*

Creative Arts and Mental Disability: The Role of the Creative Arts in the Development of Young People and Adults with Mental Handicaps and Severe Profound or Multiple Disabilities. Edited by Stanley S. Segal. Bicester, Oxon: A.B. Academic Publishers. 1990. 115 pp. £15.95.

This book describes the proceedings of an International Symposium and Festival of Arts held in London at the King's Fund Centre and the Cockpit Theatre exploring the creative arts with people with mental disabilities.

The papers presented are diverse in style and content. The first three describe how the symposium was set up with a parallel programme of performing arts at the Cockpit Theatre. Professor Segal then provides an informative account of the development of special education and integration of the arts into this from an international perspective.

Poitevan writes an exciting chapter on how seeing people with mental disabilities being creative is a potent method for changing attitudes, and that such expression can be used by those with disabilities to reveal difficulties within the organisations or institutions that they are involved with. This may, of course, be quite a challenge to those institutions. He also describes the challenge to the individual with a disability, in that coming to terms with newly discovered aspects of themselves may be threatening and requires the individual to be supported.

Poitevan writes from his own experiences but some of the other authors' experiences do not directly relate to this client group. This makes their writing less powerful. This is not the case, however, with Taylor, who describes with great enthusiasm and lots of examples, how the arts allow the expression of emotion and so facilitate change, which may take many forms, such as, in self-image, concentration and skills. As an experienced counsellor and speech therapist she describes her work in the UK with people with mental disabilities, and her experiences in Israel.

This book is interesting to dip into. The importance of leisure activities and the creative arts is recognised by us all, but is sometimes neglected when thinking of the needs of people with disabilities. This book will be a welcome addition to the libraries of those working in this field. It is short, easy to read and some chapters are outstanding.

GERALDINE HOLT, *Consultant Psychiatrist, Goldie Leigh, Lodge Hill, London*

The Roles and Tasks of Community Mental Handicap Teams. Edited by STEPHEN Brown and GERALD WISTOW. Aldershot, Hampshire: The Press Office. 1990. 130 pp. £25.00.

This slim volume is the report of a conference in Loughborough in 1986, organised by the Centre for Research in Social Policy at Loughborough University and the British Institute of Mental Handicap, when the two editors were Research Fellow and Co-Director of that Centre. The conference proceedings are readable, interesting and appear to lose nothing in the transcript. It does, however, seem a pity that over three years have passed since the conference, but there is still much that is pertinent today.

Community teams started around the early 1980s when community-care needs were being addressed, and effective delivery of care in the community was to be the antidote to a decade of poor and fragmented services in institutions. It is also important to remember that multidisciplinary teams were used first in mental handicap services while teams in other services such as general psychiatry and drug addiction have followed in their wake.

If community teams are indeed the linchpin of the community-based service then they cannot afford to be fragile or vulnerable in the hands of the ignorant or powerful. The honeymoon is over and teams must address their dynamics and the work done, with sophistication, as in this text, so that service delivery to the client and carers is the best that can be offered within the resources and done with informed inspiration.

There is no one model for such a team, a matter of strength in my view but of concern for some. In some services community teams are at the periphery of another strong part of the service while in other places the team may represent the total service. Some teams have a planning function and others do not. What seems clear is that audit must now be part of the work of any team.

Teamwork is never easy but this book can help teams to remedy their ills and, for robust teams, point the way to further endeavours. It is a thoroughly useful book for teams to own and for libraries to stock. There will be few who will buy this text for themselves for a price that can only reduce the size of an already small market.

JOAN BICKNELL, *Professor Emeritus in the Psychiatry of Mental Handicap, St George's Hospital Medical School, London*

A DSM-III-R Casebook of Treatment Selection. By SAMUEL PERRY, ALLEN FRANCES and JOHN CLARKIN. New York: Brunner/Mazel. 1990. 416 pp. $42.50.

Although the DSM classification system in psychiatry has received great support among research psychiatrists and been a major influence on the revised psychiatric classification in the *International Classification of Diseases*, it continues to attract criticism from clinicians. Despite formal diagnoses using the DSM classification being mandatory in many parts of North America, the labelling process is often seen as a sterile academic exercise that serves the whims of bureaucracy but is of no value to the patient.

This book, together with its predecessor, *Differential Therapeutics in Psychiatry* (1984) aims to put flesh on the DSM skeleton. It adopts a standard format whereby each of 53 cases is described in terms of five axes; the setting where the treatment occurs, the format indicating who takes part in the treatment (varying from individual to family therapy), the time taken to complete treatment and the frequency of sessions, the approach (which describes the range of psychological interventions from the behaviour therapy to psychoanalysis) and somatic treatment involving drugs and electroconvulsive therapy (ECT). The description of the 53 cases is helped by including guest contributors in certain fields and by selecting historical cases from Alzheimer, Kraepelin, Freud and Cleckley.

Their first book was a great success and I am sure the second will be also. The authors write with great good humour and pick on eye-catching titles for the cases which appear to have been derived from the detective novels of Erle Stanley Gardner. Each case is described by a title indicating its key elements, after which our three 'Perry Masons' analyse and dissect it with gusto before constructing a plan of treatment and in some cases describing the actual outcome. Books that concentrate on case histories sometimes fall to the level of caricature in which the descriptions fit the author's requirements so well that they are clearly artificial. Dr Perry and his colleagues are too honest to fall into this trap; they give descriptions that are stamped with veracity – I particularly liked the Case of Harry the Turtle (schizotypal personality disorder) and that of the Once-Contented Car Washer (undifferentiated schizophrenia) – and the subsequent descriptions are written with sensitivity and understanding. Many psychiatrists now like to think of themselves as eclectic in their therapeutic approaches but in practice few are. The analysis of the cases demonstrates the true value of eclecticism and the integration of the different approaches is carried out so cleverly that there are no seams between them. The only addition I would make is one to illustrate that DSM does not cater for all cases. We need the Case of the Difficult Diagnosis to show that even DSM can sometimes lead us astray!

I heartily recommend this book to those who wish to see American classification in action. It is instructive and stimulating and ideal for educational purposes. In the preface the authors also state that the book was intended from the start to be fun. They succeed in this aim so we can all laugh as we learn.

Peter Tyrer, *Senior Lecturer in Community Psychiatry, St Charles' Hospital, London*

Towards a New Personality. By Theodore Millon. New York/Chichester: Wiley. 1990. 200 pp. £24.50.

Personology is attracting new interest, although the relation of this work to that of Murray is often not entirely clear. Millon in this volume has attempted to develop a new personological theory that has a direct bearing on personality disorders which are of increasing importance in American psychiatry.

Millon claims that his theory is embedded in modern biology and science and there is reference to the second law of thermodynamics, sociobiology, r and κ strategy, catastrophe theory and chaos and the bipolarity in the psychological theorising of Freud, Eysenck and Gray, *inter alia*. From all this discussion Millon claims that three bipolar dimensions underlie personality – "pleasure–pain, passive–active and self–other", this last being confirmed both by biology and Greek mythology. Having established these polarities, Millon shows how they apply to the DSM–III–R axis-II personality disorders and then discusses the tests which claim to measure these polarities. One of them is of great interest to the theory – the Millon Personality Type Questionnaire, but no details of this test are given which are still in press.

This reviewer finds it hard to evaluate this book. The theory is bold and embraces much, if not all, of personality, yet no details of its empirical basis are given. Conceptually I remained unconvinced because in this field notoriously the warning *tot homines quot sententiae* is always true.

Furthermore, the style *is* unnecessarily abstract and I fear pompous yet at times bathetic. We are told that it is women that become pregnant not men, for example. This is a pity because the theory is interesting and I think that Millon, who was trying to emulate Freud's project and Wilson's sociobiology, was ill served by such lofty ideals. Nevertheless, in brief, an interesting but annoyingly difficult book.

Paul Kline, *Professor of Psychometrics, University of Exeter*

Vandalized Lovemaps: Paraphiliac Outcome of Seven Cases in Paediatric Sexology. By John Money and Margaret Lamacz. Buffalo, NY: Prometheus Books. 1990. 224 pp. £18.50.

This is the age of sexual counter-reformation which has (whatever information made sex positive and permissible) made sex negative and heretical. Thus, commercialisation of sex, the professionalisation of victimology leading to abuse by the social scientists, and the pathologisation of sex by inventing sexual addiction are the three main strategies of the sexual counter transformation. This, as Money & Lamacz argue, has put paid to the advancement of the science of sexology, especially the paediatric one. In this book they develop the theme of 'lovemap' further by giving detailed case histories of seven of the patients who have attended the paediatric and endocrinal clinics at the Johns Hopkins University.

Lovemaps was a concept developed by Money in 1986. He postulates a lovemap as a functional and developmental template that functions in mind and brain. This template presents an idealised programme of sexuo-erotic activity in imagery and/or actual performance. Since paraphiliac lovemaps are said to be stable over a life time, the whole treatment plan therefore has to be preventive. It is a fascinating concept and Professor Money deserves congratulations on this alone.

However, vandalisation of these lovemaps is an entirely different matter. Vandalisation is normally defined as the wanton or deliberate destruction. Where the lovemaps exist fully formed, such destruction cannot be deliberate because Money & Lamacz are putting forward a theory of vandalism as a non-deliberate act. The authors have not clarified the exact role of psychodynamic versus physical or organic factors in their cases. Of the seven cases they report, five have sex-organ anomaly. Thus the cards are already stacked against them. Alas, they ignore the paraphiliac cases who do not have sex-organ or other physical anomalies but still have, in street parlance, 'kinky sex' or 'perversions'. Indeed it is a first step in recognising aetiological factors in an under-researched field, but the style and the contents of the book make it difficult to read. The concept of lovemaps deserved to be developed further but unfortunately vandalised lovemaps will have a very limited appeal to a very limited audience.

Dinesh Bhugra, *Lecturer, Institute of Psychiatry, London*

The Craft of Psychotherapy. Twenty-seven Studies. By I. H. Paul. New Jersey: Jason Aronson. 1989. 307 pp. $30.00.

This book has an unusual structure. Paul, a psychoanalyst working in New York, echoes the verbal exchange that is central to the practice of psychoanalytic psychotherapy by casting his text in the form of a dialogue between the reader – an informed learner – and a teacher, with the author in his expert role as supervisor and practitioner. This dyadic exchange brackets sections of dialogue between patient and therapist, some of their possible responses to each other and an examination of the meaning. All this may appear more complicated than it is. The book is divided into seven sections: the psychotherapist's craft, basic instruction, business, interpretation, timing, what to interpret when, and resistance. Within these sections are the 27 studies of the subtitle. Therapists experienced in dynamic psychotherapy will instantly recognise the frequently encountered, tense scenarios explored in these studies. Examples are: "But you're the therapist!", "But what good is that?", "It's embarrassing", "I am bothered by you sitting there and staring at me", "Am I like your other patients?" and, unsettlingly, "You do have a supervisor, don't you?"

Most dialogical books are diabolical to read. Either you cannot find the topic you are interested in or the question is not in the form you want. For the most part, Paul has avoided these pitfalls. He has drawn on his extensive experience of supervising therapists at an early stage in their training and deals sensitively and encouragingly with many of the problems of the method. He also has a clear idea about the method that he is teaching. The basic instruction is for the therapist to be minimally directive; this stance informs the patient that he can talk about the things he wants to talk about and that the therapist will listen, will try to understand and, when he has something useful to say, will say it. Great emphasis is placed on neutrality with respect to content. This is not to say that the therapist does not have preconceptions about what would be helpful for the patient to explore, but he tries to avoid imposing these predilections on the patient, allowing as far as is humanly possible a free choice of topic. A frame is then set which facilitates the reflective examination, so characteristic of the psychoanalytic method, of how the patient chooses – or is transferentially impelled – to use the session. A useful distinction is made between business and narrative, the former encompassing practical matters of fee, schedule and procedure that contribute to the structure of therapy, the latter being the stuff of therapy. Business should be dealt with directly and without interpretation, which is reserved for narrative.

The predilection of this reviewer is for a more humanistic, interpersonal style of therapy, but there is no doubt that that advocated by Paul places the needs and concerns of the patient centre stage and fosters their close examination. The therapist scrutinises carefully the departures from neutrality. Paul ably illustrates the way in which neutrality means not taking sides, either with people in the patient's life or with aspects of the patient's self. To do this well requires discipline and dedication. This is a useful text for supervisors and novices.

Mark Aveline, *Consultant Psychotherapist, Nottingham Psychotherapy Unit*

Ending Men's Violence Against their Partners. By Richard A. Stordeur and Richard Stille. London: Sage Publications. 1989. 320 pp. £29.25 (hb), £13.95 (pb).

The authors of this book advise their readers to use it as a practical guide to the group treatment of men who batter their partners. The text is divided into four parts, the first of which covers theoretical perspectives and gives a brief overview of historical and social aspects of violence against women by men and the development of specialised treatment programmes for the male perpetrators. Social, psychological and feminist/political theories of wife battering are outlined, and a comprehensive catalogue of characteristics typical of the batterer himself is discussed.

Part II, headed "Individual contacts", describes assessment procedures and crisis intervention.

In Part III group treatment is described. The closed group is psychoeducational in orientation and the leaders are directive. Typically, batterers have little awareness of their emotions, have poor communication skills and grew up in families where violence was used by the father as a way of controlling his partner. The batterer does not usually take responsibility for his behaviour and blames the victim for the violent outbursts. Acts of violence and the consequences are minimised. Treatment, then, requires the group members to share accounts of their violent behaviour with each other, to think about it, examine their attitudes and rationalisations, and in a series of structured exercises and discussions learn how to identify their feelings, identify triggers for violent behaviour and learn new, adaptive ways of handling intimate relationships. Treatment involves 24 to 32 sessions. Worthwhile results are reported. The final section deals with counsellor's issues.

This book is excellent and will no doubt become a definitive text on the subject of group treatment of men who batter their partners. The writing style is clear, concise and easy to read. I strongly recommend the book to all mental health professionals who are required to deal with such men.

STEPHEN P. REILLY, *Consultant Psychiatrist with Special Responsibility for Psychotherapy, Bootham Park Hospital, York*

Dilemmas and Difficulties in the Management of Psychiatric Patients. Edited by KEITH HAWTON and PHILIP COWEN. Oxford: Oxford University Press. 1990. 257 pp. £35.00.

This book is the first in a series stemming from an interesting idea. Each of the contributors was invited to a conference to give a paper on one topic, which subsequently became a chapter. The editors should be congratulated that this turned out to be possible as anyone who has ever tried getting manuscripts from conference presenters will know. The manuscript was sent in advance to one of the other participants who became the discussant at the conference. After the conference the original author modified the paper, if necessary, in the light of the comments from the discussant and the audience. This must have been a lot of work for the editors, but they have produced a first rate practical volume which will be useful to many practising psychiatrists. The main thing in its favour is that it concentrates on real contemporary dilemmas and debates in management, some, but by no means all of which will be familiar.

The book has four chapters on the physical treatment of affective disorders, treatment of resistant depression and mania, the use of the monoamine oxidase inhibitors, and when to think of psychosurgery. There are two chapters on alternatives to medication for anxiety and depression.

There are then three chapters on the prevention of suicide, the prevention of self-harm and the most appropriate response from psychiatrists to the suicidal patient. Schizophrenia has a fair slice of the book with the management of persistent symptoms, prevention of tardive dyskinesia and the use of ECT having good discussions.

Violence towards women is a big issue and a chapter on overcoming the effects of childhood sexual abuse, and another on rape make interesting, if inconclusive, reading.

A miscellaneous group of chapters deal with such diverse subjects as dangerousness, the use of drugs for personality disorders, treatment of alcohol dependence, the psychiatrist's role in HIV-related disorders, chronic fatigue syndrome and the disclosure of confidential information.

While this might seem a bit of a hotchpotch of subjects, I found myself turning from one chapter to the next with interest. This is largely because the chapters are authoritative and each ends with clear clinical guidelines, which at least makes you feel you have learned something of practical use. Sometimes this feeling is illusory, but that relates more to the topics, some of which do not lend themselves to this kind of treatment, than to the editors or the contributors. This is a book which most psychiatrists will find interesting and useful.

CHRISTOPHER THOMPSON, *Professor, Department of Psychiatry, Royal South Hants Hospital, University of Southampton*

The Quality of Life. The Missing Measurement in Health Care. By LESLEY FALLOWFIELD. London: Souvenir Press. 1990. 234 pp. £12.95 (hb), £8.95 (pb).

The title of this excellent book describes the author's philosophy. She recounts poignantly the conversation which led to her writing the book. A young friend who died of leukaemia asked "why I had not tried to dissuade her from a therapy with poor chances of survival, but a high chance of destroying the quality of whatever life she had left". In the introduction she further emphasises her position. "There are actually states of life that are worse than death."

The author presents a thorough review of the literature. As the book is written for a lay as well as a professional readership, the medical reader will have to endure some simplistic and occasionally inaccurate descriptions of common conditions.

The author outlines four core domains in which quality of life should be measured – psychological, social, occupational and physical. She continues by discussing some of the many methodological issues involved in trying to measure the quality of life and discusses critically a number of different measurements already in use. (The book would be worth obtaining for this chapter alone for those clinicians who intend to become involved in this field.)

In the following five chapters Fallowfield discusses issues relating to the quality of life in cancer, AIDS, cardiovascular disease, arthritis and the elderly. She is quite rightly scathing in her condemnation of the virulent, unpleasant epidemic of sanctimonious moralising which has accompanied the AIDS epidemic. In these chapters and in the chapter on the 'Quality of dying', the author discusses the psychosocial problems which patients and their carers encounter. This is an area in which there is a major role for the liaison psychiatrist in improving communication, being honest with the patient and the relatives rather than colluding, and developing and providing an appropriate means of support and care for relatives and patients. This would seem to me to be a far more valuable way of using the time of a liaison service instead of assessing parasuicides, the majority of which could be assessed by junior physicians.

The chapter entitled "The quality of dying" begins with the following quotation from Colin Murray Parkes: "Medicine should not confine itself to the prevention of death, any more than family planning should confine itself to the prevention of birth". Many doctors are unable to cope with this inevitable aspect of illness.

The next chapter looks at the quality of life from the health economist's viewpoint. The book concludes with a plea that the immeasurable aspects of life should not be ignored in the new world of statistical analyses and cost comparisons.

This is an excellent book which is of equal value to the professional and lay reader. It should be read by all practising doctors. Perhaps more importantly, the philosophy within should be taught in medical school and given at least as much prominence in the curriculum as the more heroic side of medicine.

OSCAR DALY, *Consultant Psychiatrist, Downshire Hospital, Downpatrick, Co. Down, Northern Ireland*

Strangers at Home: Vietnam Veterans Since the War. Edited by CHARLES R. FIGLEY and SEYMOUR LEVENTMAN. New York: Brunner/Mazel. 1990. 416 pp. $26.95.

Twenty authors from various backgrounds contribute to this collection of writings on the experiences of Vietnam veterans since the war. The unique nature of the Vietnam conflict is described well, and the reader gains great insight into the increasingly ambivalent and negative attitude of the US nation towards the war as it progressed, resulting in the returning veterans being stigmatised and feeling alienated. Reference to veterans of other wars highlights the universality of many of the post-war experiences.

The book is divided into three sections, the first of which considers the war itself and those who fought in it. The chapter by Smith on "Oral history" is particularly gripping, especially the verbatim account of a Marine interrogator describing both the difficulties he faced in Vietnam and the let-down he felt on his return. The second section deals with the returning veterans readjusting to US society, including accounts of research carried out into their estrangement, psychosocial readjustment, and employment experiences. My favourite passage in this part of the book is Wilson's account of the war's effects on the personality development of the many adolescent soldiers. The final section looks at the actions of the government and other agencies. Stanton's chapter on drug use and Bitzer's account of the mistreatment of many veterans suffering mentally as a result of the conflict make good reading. The appendix to Bitzer's chapter is the memorandum advising use of the term 'post-traumatic disorder' in place of 'post Vietnam syndrome' emphasising that this is not restricted to Vietnam veterans.

In conclusion, this book might be of interest to those dealing with war veterans and indeed others involved in major traumatic events. Overall it is well written and easy to read. The multidisciplinary authorship ensures varied perspectives, including economic, psychological and sociological viewpoints. It gives a broad, detailed and comprehensive picture of the Vietnam veteran since the war. Its only drawbacks are a tendency to repetition at times and the occasional American word or phrase which is difficult to understand.

JONATHAN BISSON, *Registrar in Psychiatry, Queen Elizabeth Military Hospital, Stadium Road, London*

Substance Abuse and Dependence. By HAMID GHODSE and DOUGLAS MAXELL. London: Macmillan Press. 1990. 262 pp. £37.50 (hb), £14.95 (pb).

The need for 'caring professions' to have knowledge and occupation-specific skills in dealing wih substance misuse problems is not in question, but latching onto the right educational message is not so easy. Within a training programme, a mix of specialist and generic input can go side by side, complementing each other, but in a book this is more difficult to achieve. This book is billed as a practical guide for a wide range of professionals, students and other workers within the field and should therefore be judged against its relevance to those groups and the effort given to addressing their needs.

The book is divided into four parts. Part 1, "Identifying the problem", gets off to a shaky start with a chapter defining the nature of dependence: I am certainly prejudiced in that this is not my idea of dependence, but while the specialist might follow this text with interest I suspect the target readership will be confused. Another chapter on "Substance misuse careers", is particularly well written and instructive, however. Part 2, "Treatment and management", is perhaps the most balanced section, all three chapters are very readable and informative. The chapter on "Psychosocial interventions" is particularly attentive to the consumer. Part 3, " Complications of substance abuse", has an excellent summary of medical complications which is well pitched for practitioners dealing with addiction problems. In contrast, the chapter on "Psychiatric problems" lacks depth and useful framework. Part 4, "Preventive issues", is rather patchy on prevention but finishes with a chapter, "Drugs and the law", which admirably, and almost single handedly, takes on the stated brief of offering a practical guide.

In summary, this is a competent text rather more for the professional within the field than the non-specialist. It is disappointing in that the combined experience and talent of the authors is capable of producing something much better. As often happens with multiple authorship there is irritating overlap and a failure to excite the reader with a clear direction and approach. I think it is also disappointing that the target readership are unlikely to find this the practical guide that was promised.

DUNCAN RAISTRICK, *Leeds Addiction Unit, Clarendon Road, Leeds*

The Workplace Within: Psychodynamics of Organisational Life. By LARRY HIRSCHHORN. Massachusetts: MIT Press. 1988. 265 pp. £8.95.

In this book the author develops a psychodynamic concept of work life by linking his consulting experience in organisations to a theory of work in post-industrial society. He argues that in a post-industrial setting it is increasingly difficult to maintain group cohesion while remaining open to influence and information from outside the group. Social defences, which may involve processes such as splitting, projection and introjection, are acknowledged as a means of containing such anxiety.

Routines and structures are developed by organisations to handle uncertainty. Hirschhorn suggests that because classical organisation theorists have not linked the experience of uncertainty in the organisation to the individual's feelings of anxiety, they have posed the issue of an organisation's uncertainty too narrowly and have then proposed solutions that rely on such rational methods as mathematical calculation and organisational design. When anxiety intrudes, rational processes are distorted by irrational processes.

As the anxiety at work grows, people need to project their sense of persecution onto others. By using Klein's theory of reparation in the workplace, the production of valued goods and services for others provides a framework for repairing relationships. Industrial society makes reparation difficult by conflating the good or the ideal with the symbol of a punishing authority, by substituting guilt for shame and by confusing limitation with sin. This constellation leads to emphasising triumphs over others. Hirschhorn argues that society has reached cultural, technical and ecological limits in its capacity to sustain the psychodynamics of triumph.

To acknowledge the new, integrated complexity of a post-industrial world, people may need to understand how society as a whole values the goods and services it produces.

This thought-provoking book is ambitious in that it addresses work both at a personal level and in the wider context of society. It is clearly written for a wide audience with respect for the reader who is invited to take up the interpretive method where the author's explanations seem incorrect or incomplete. It is an interesting book which deserves to be widely read.

LORNA ARBLASTER, *Research Fellow, Department of Public Health Medicine, University of Leeds*

Why Children Reject School: Views from Seven Countries. Edited by COLETTE CHILAND and J. GERALD YOUNG. New Haven: Yale University Press. 1990. 229 pp. £25.00.

This is the 10th volume in the series "The Child in His Family, The Yearbook of the International Association for Child and Adolescent Psychiatry and Allied Professions". It was produced for the 12th International Congress of the International Association, held in Japan in 1990.

The emphasis is on absence from school. There is an excellent review of school refusal by Lionel Hersov, and a good review of school attendance problems more generally by Richard Landsdown, although he gets the Leeds Truancy Project wrong: it was children taken to court there not parents. The final chapter by J. Gerald Young and others is well worth looking at; I was particularly pleased to be reminded that haloperidol can sometimes induce symptoms of school refusal, or work refusal in adults, and that there is evidence for depressive symptoms occurring secondary to a variety of childhood disorders, not just school refusal.

The five chapters from Japan provide an interesting, although somewhat peripheral, introduction to the particular problems children there experience in response to their competitive educational system; school refusal in Japan is less characterised by difficulties separating from the family than it is in Western countries. The book also gives one a fascinating glimpse of German, Danish and Brazilian approaches. The three chapters written by eminent child psychiatrists in France were more concerned to restate psychoanalytic views than to provide information on absence from school in that country, although Colette Chiland's detailed description of the French education system is of interest.

I do not know how many good chapters are needed to make a book of this sort worth buying, either for yourself or for a library. Although there are some very interesting contributions, I suspect this book will mainly be for reference.

IAN BERG, *Consultant in Child and Adolescent Psychiatry, The General Infirmary at Leeds, Leeds*

Contents of *The American Journal of Psychiatry*

April 1991 Volume 148

Editorial

Whatever happened to insomnia (and insomnia research)? *Mark R. Pressman* 419

Special Articles

Origins of *DSM–I:* a study in appearance and reality. *Gerald N. Grob* 421
Subtyping *DSM–III–R* primary insomnia: a literature review by the DSM–IV work group on sleep disorders. *Charles F. Reynolds III, David J. Kupfer, Daniel J. Buysse, Patricia A. Coble and Amy Yeager* 432
Biological correlates of mental activity studied with PET. *Nora D. Volkow and Laurence R. Tancredi* 439

Regular Articles

Monitored conditional release of persons found not guilty by reason of insanity. *Joseph D. Bloom, Mary H. Williams and Douglas A. Bigelow* 444
Effects of statutes requiring psychiatrists to report suspected sexual abuse of children. *Fred S. Berlin, H. Martin Malin and Sharon Dean* 449
An empirical study of diagnostic criteria for delirium. *Benjamin Liptzin, Sue E. Levkoff, Paul D. Cleary, David M. Pilgrim, Catherine H. Reilly, Marilyn Albert and Terrie T. Wetle* 454
Diagnosing dissociative disorders in the Netherlands: a pilot study with the structured clinical interview for *DSM–III–R* dissociative disorders. *Suzette Boon and Nel Draijer* 458
DSM–IV: a nosology sold before its time? *Mark Zimmerman, V. Chowdary Jampala, Frederick S. Sierles and Michael Alan Taylor* 463
Neuropsychological performance in medicated and unmedicated patients with Tourette's disorder. *R. A. Bornstein and Victoria Yang* 468
Relations among clinical scales in schizophrenia. *Raquel E. Gur, P. David Mozley, Susan M. Resnick, Stephen Levick, Roland Erwin, Andrew J. Saykin and Ruben C. Gur* 472
Familial, obstetric, and other clinical correlates of minor physical anomalies in schizophrenia. *Eadbhard O'Callaghan, Conall Larkin, Anthony Kinsella and John L. Waddington* 479
Relation of CSF neurotensin concentrations to symptoms and drug response of psychotic patients. *David L. Garver, Garth Bissette, Jeffrey K. Yao and Charles B. Nemeroff* 484
Outcome of involuntary medication in a state hospital system. *Francine Cournos, Karen McKinnon and Barbara Stanley* 489
Clinical features of cocaine-induced paranoia. *Sally L. Satel, Steven M. Southwick and Frank H. Gawin* 495
Lymphocyte glucocorticoid receptor number in posttraumatic stress disorder. *Rachel Yehuda, Martin T. Lowy, Steven M. Southwick, Dottie Shaffer and Earl L. Giller* 499
Salivary cortisol levels and their correlation with plasma ACTH levels in depressed patients before and after the DST. *Rosa Galard, Jose M. Gallart, Roberto Catalan, Simon Schwartz, Jose M. Arguello and Jose Maria Castellanos* 505
Treatment of seasonal affective disorder with green light and red light. *Dan A. Oren, George C. Brainard, Scott H. Johnston, Jean R. Joseph-Vanderpool, Elizabeth Sorek and Norman E. Rosenthal* 509
Cardiovascular effects of bupropion in depressed patients with heart disease. *Steven P. Roose, Gregory W. Dalack, Alexander H. Glassman, Sally Woodring, B. Timothy Walsh and Elsa Grace V. Giardina* 512
Controlled discontinuation of benzodiazepine treatment for patients with panic disorder. *Russell Noyes, Jr, Michael J. Garvey, Brian Cook and Michael Suelzer* 517
Suicide, stressors, and the life cycle. *Charles L. Rich, Gary M. Warsradt, Robert A. Nemiroff, Richard C. Fowler and Deborah Young* 524

Clinical and Research Report

Potential HIV exposure in psychiatrically hospitalized adolescent girls. *Dewleen G. Baker and Douglas Mossman* 528

Contents of *The Journal of Nervous and Mental Disease*

April 1991 Volume 179

Comorbidity of psychiatric disorders and personality profiles of American World War II prisoners of war. *Brian E. Engdahl, Nancy Speed, Raina E. Eberly and Joseph Schwartz* 181

Brief psychotherapy of personality disorders. *Arnold Winston, Jerome Pollack, Leigh McCullough, Walter Flegenheimer, Richard Kestenbaum and Manuel Trujillo* 188

Reasoning in deluded schizophrenic and paranoid patients: biases in performance on a probabilistic inference task. *P. A. Garety, D. R. Hemsley and S. Wessely* 194

Hospitalization and the cognitive deficits of schizophrenia: the influences of age and education. *Gerald Goldstein, Joseph Zubin and Michael F. Pogue-Geile* 202

The use of cognitive behavior therapy with a normalizing rationale in schizophrenia: preliminary report. *David G. Kingdon and Douglas Turkington* 207

Discontinuation of neuroleptic medication in older, outpatient schizophrenics: a placebo-controlled, double-blind trial. *Paul E. Ruskin and Gary Nyman* 212

Early treatment time course of depressive symptoms in opiate addicts. *Eric C. Strain, Maxine L. Stitzer and George E. Bigelow* 215

Urine screening practices in methadone maintenance clinics: a survey of how the results are utilized. *Donald A. Calsyn, Andrew J. Saxon and D. Christopher Barndt* 222

A retrospective outcome study and review of hypnosis as treatment of adults with sleepwalking and sleep terror. *Thomas D. Hurwitz, Mark W. Mahowald, Carlos H. Schenck, Janet L. Schluter and Scott R. Bundlie* 228

Brief Report

Carbamazepine for high dose diazepam withdrawal in opiate users 234

Books. Vasilyuk, F. *The Psychology of Experiencing*; *Communicating with Medical Patients*; *Alzheimer's Disease: Treatment and Long-Term Management*; *Contemporary Approaches to Psychological Assessment*; *Men in Therapy: The Challenge of Change*; *Suicide Over the Life Cycle: Risk Factors, Assessment, and Treatment of Suicidal Patients*; *Aging in a Technological Society*; *Neurobehavioral Aspects of Multiple Sclerosis*; *The Psychological Aspects of Chronic Illness*; *Slow Wave Sleep: Physiological, Pathophysiological and Functional Aspects*; *The Financing of Biomedical Research*; *Social Control of the Drinking Driver* 235

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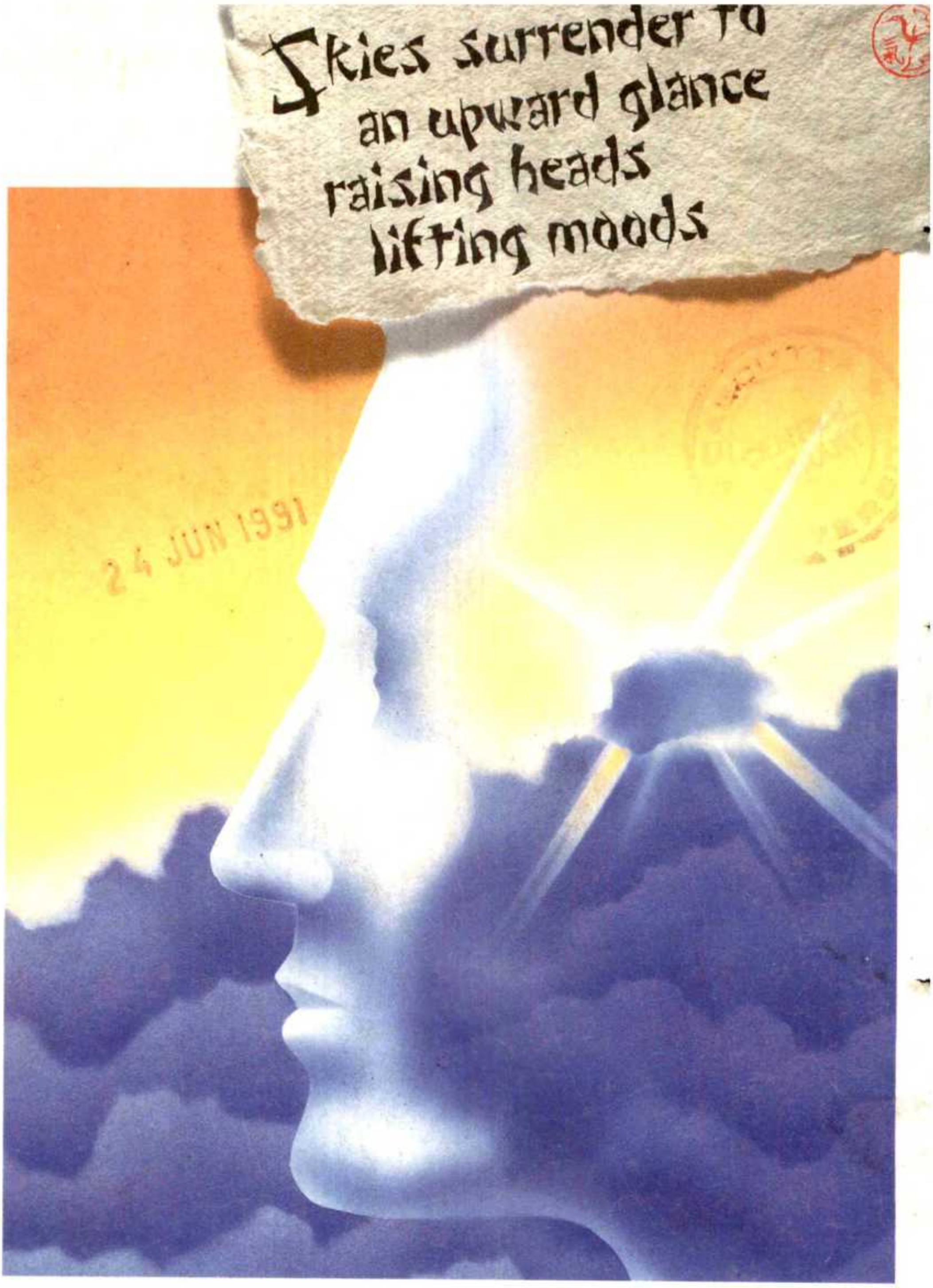

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Contents

List of contributors 5

Introduction
LYN PILOWSKY, GERALDINE O'SULLIVAN, RAJINI RAMANA, ELENI PALAZIDOU and PARIMALA MOODLEY 7

Emerging issues in medical ethics
CAROL C. NADELSON 9

Issues for women in the development of mental health services
FIONA SUBOTSKY 17

Depression in women
E. S. PAYKEL 22

Psychotropic drug prescribing in women
HEATHER ASHTON 30

Alcohol and drug misuse among women—an overview
EDNA OPPENHEIMER 36

Life stress and post-partum psychosis: a preliminary report
M. N. MARKS, A. WIECK, S. A. CHECKLEY and R. KUMAR 45

Women as perpetrators and victims of crime. A sociological perspective
FRANCES M. HEIDENSOHN 50

Adult sequelae of child sexual abuse
CAROL SHELDRICK 55

Sexual abuse, disordered personality and eating disorders
L. McCLELLAND, L. MYNORS-WALLIS, T. FAHY and J. TREASURE 63

Gender differences in carers of dementia sufferers
ROBIN G. MORRIS, ROBERT T. WOODS, KATH S. DAVIES and LORNA W. MORRIS 69

Sex differences in service usage in long-term psychiatric care. Are women adequately served?
RACHEL E. PERKINS and LEN A. ROWLAND 75

Where do people with long-term mental health problems live?
ALISON M. CONNING and L. A. ROWLAND 80

Psychology and psychopathology in women—a psychoanalytic perspective
ESTELA V. WELLDON 85

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Editors' Introduction

LYN PILOWSKY, GERALDINE O'SULLIVAN, RAJINI RAMANA,
ELENI PALAZIDOU and PARIMALA MOODLEY*

> "If you want to know more about femininity, enquire from your own experiences of life, or turn to the poets, or wait until science can give you deeper and more coherent information."
> (Sigmund Freud, 1933)

Since the 1960s there has been a rapid increase in research literature pertaining to women. This was a departure from previous conceptualisations of women's mental health. Seiden (1976) referred to this as a 'revolution' in women's studies "unequalled in any other field related to psychiatry".

Showalter (1987) examined the history of women, madness, and English culture. Darwinian ideas influenced psychiatric thought from the late 19th century to World War I. One of the foremost early British psychiatrists, Henry Maudsley (1835–1918), embraced the view that biology determined destiny; he insisted that "there is sex in mind as clearly as there is sex in body". Indeed, female physiology marked women "for very different offices in life from those of men". Showalter demonstrates how theories of sexual differences elaborated by Darwinian science were "incorporated into a highly prescriptive late Victorian psychology of women." Rigidity towards sex differences and gender roles proved surprisingly persistent, even into the 1970s: Showalter is able to quote from a 1972 textbook on psychiatry, recommending psychosurgery for a depressed woman "who may owe her illness to a psychopathic husband who cannot change and will not accept treatment". British psychiatry has been slow to acknowledge the relevance of specific studies of female psychology and psychopathology to increasing understanding of mental disorder (in both women and men).

In contrast, the American psychiatric establishment has been more successful in assimilating, and distributing, the information gained through this research. In 1972, the American Psychiatric Association set up a task force on women. Over the following decade, the *American Journal of Psychiatry* published two special sections dealing with women's issues. In one of these sections, Benedek (1981) commented that the previous eight years had seen major changes in beliefs and expectations as to women's and men's roles in society which would need to be incorporated into psychiatric education and treatment. Although women were the major mental health service consumers, their special needs had yet to be understood and accounted for in service planning. The hope in publishing a section devoted to women was to provide enlightenment, revitalise attitudes and attract a continuous flow of research contributions dealing with the 'new psychology of women'.

Over the last 30 years, attitudes have altered significantly. Gender roles and biological sex differences are no longer equated. There is a plethora of research into sex difference in mental illnesses and the way in which social expectation and gender roles affect mental health of both men and women. Yet women are still more likely than men to need psychiatric help, and bear the increasing burden of community care of the mentally ill.

It is timely, therefore, to examine aspects of psychiatric disorder in women. This supplement represents a selection of papers from the first International Conference on Women and Mental Health, held at the Institute of Psychiatry, London. The conference provided a forum in which the particular mental health needs of women could be discussed in a multidisciplinary setting.

The supplement brings together reviews and current research on topics relating to women and mental health, ranging from a psychoanalytic view of women's psychology/psychopathology, a sociological perspective on women and crime, and psychiatric investigations into mental illness in women and its impact on women carers in the community.

The debate on mental health issues for women continues. We hope that this collection of papers will stimulate yet more discussion and research. The interest generated by the inaugural conference has been maintained – the second International Women and Mental Health Conference and the Conference on Women and Substance Abuse were both held at the Institute of Psychiatry in March 1991.

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*The editors of this supplement comprised the Organising Committee of the 1st International Conference on Women and Mental Health.

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Emerging Issues in Medical Ethics

CAROL C. NADELSON

Ethical principles are influenced by personal values and beliefs, and by societal context. They are not immutable. In medicine, as new technologies have developed and changes in health-care delivery have resulted, historically held views about the responsibilities, obligations and relationships between health-care providers and patients have been challenged.

The increasing complexity and cost of new technology, coupled with limited resources to provide care for all those who need or want it, creates new ethical dilemmas. These are related to the need for decision-making based on competing priorities, without established policies regarding who should make decisions and what the guiding principles should be. Current codes of medical ethics appear to be inadequate to address today's emerging questions because values and ethical systems vary widely and often conflict. Choices that enable one to preserve personal moral accountability in a pluralistic society are difficult to make.

Further, the process of medical decision making, as well as the delivery of medical care, is increasingly directed by those whose ethical frameworks do not originate from health-care training or practice. This affects decisions and their implementation. For example, a businessman running a private hospital does not expect to deliver care in the same way as a charitable institution. He is bound by the interests of his investors and not primarily by a concept of public good. The computerisation of medical records and requirements for disclosure of diagnostic and treatment data in order to provide reimbursement makes the transfer of confidential information routine. The concept of consent is altered by the financial pressure on individual patients to permit disclosure.

Medical ethics encompass an enormous range of issues. In this paper, I focus on aspects of current and emerging concerns, particularly some that relate specifically to women. Recognising that overt as well as subtle cultural differences exist, my major reference is to the United States.

Changing codes of medical ethics

Codes of medical ethics have existed since ancient times and have varied with culture and era. The Hippocratic Oath was unique in emphasising the cure of the patient as the single over-riding responsibility of the doctor. Subsequently, medical ethics has also been concerned with the dignity, honour and reputation of the profession. Currently, as guiding principles, most Western countries emphasise the autonomy or self-determination of patients, a concept of beneficence which implies doing 'good' rather than merely doing no harm, a concept of justice related to access to resources, and the doctor's responsibility to his/her individual patient.

Different priorities are placed on these principles in different societies. Patient autonomy may be limited by decreasing the availability of procedures like cardiac bypass surgery. Denial of access may be based on socio-economic, age or prognostic factors; family and societal needs may outweigh the desires of the individual in certain situations, like forbidding the performance of abortion despite the wishes of a woman (Newman & Brody, 1988). Engelhardt (1986) stated "at the very roots of ethics there is a tension. It springs from the difference between respecting the freedom and securing the best interests of persons."

This raises one of the fundamental problems of medical ethics, the definition and scope of paternalism. Generally, in the ethical literature, it refers to "practices that restrict the liberty of individuals, without their consent, with a justification for such actions as either the prevention of some harm they will do to themselves or the production of some benefit for them that they would not otherwise secure" (Beauchamp, 1979). Thus the debate centres upon whether paternalistic justifications can be morally acceptable and where the limits and boundaries might be.

Other principles of medical ethics that are further elucidated in Western countries include considerations of confidentiality and the boundaries of therapeutic relationships. These areas encompass issues like valid consent and refusal on the part of the patient; the responsibilities of the doctor, including failure to appropriately inform a patient; deception in practice and research; and sexual interaction between doctors and patients.

Decisions about access to care, and rationing, are often dealt with by omission rather than by clearly-stated policies. For example, patients may not have access to certain types of care because the resources are not available in their community or because they cannot pay for them. In other situations, ambiguities around conflicting ethical principles make it difficult to be definitive about policy. For example, considerations of patient confidentiality preclude disclosure of the diagnosis of AIDS, yet not to disclose endangers the health of family members and others in the community. The policy that patients' HIV tests should be confidential has recently been vigorously debated in the US because reports of doctors transmitting AIDS to patients has resulted in public pressure to test health-care workers and disclose results (Altman, 1990).

Pellegrino & Thomasma (1988) imply that shifting ethical paradigms and conflicting moral principles may be related to some of today's health-care dilemmas. They discuss the conflicting ethical principles of health care on business, contractual, preventive, covenantal and beneficent models. From the business perspective, they suggest that medicine has been considered a commodity and the ethical obligation of doctor to patient has become that of businessman to consumer. The contractual model is an extension of this model whereby a contract formalises the relationship, protecting the patient from excessive paternalism or economic self-interest from the doctor. The preventive, or public health, model obligates the health-care provider to protect many 'healths' and does not place as high a priority on the individual doctor–patient relationship.

A different perspective derives from the traditionally held covenantal model. It is grounded in the trust and obligation between the doctor and the patient. Pellegrino & Thomasma, in re-emphasising the importance of the principle of beneficence suggest that the doctor and patient are joined because of the needs of the patient. Both partners recognise the patient's dependence upon the doctor, and the doctor's responsibility for making good and moral judgements on behalf of the patient. This model acknowledges that the patient who is ill may not be capable of totally free and informed consent or autonomy, by virtue of anxiety, fear or lack of knowledge. It is around this issue that psychiatrists have become most involved. They are often asked to assess patient competence to consent, especially when there is a question of impairment of judgement or decision-making capacity. Thus, psychiatrists may be said to act in a paternalistic fashion when they are asked to render opinions that potentially limit patient autonomy.

The nature of the covenantal relationship and the principle of beneficence call into question many current medical practices which involve the doctor in activities that may not do 'good' for the patient. These practices include the role of the doctor in the rationing of health care, as a gatekeeper or guardian of society's resources. (Nadelson, 1986; Pellegrino & Thomasma, 1988). While it is attractive from an economic point of view, serious ethical questions are raised if the doctor cannot be trusted by the patient to act in his/her best interests. If the doctor becomes a double or triple agent, acting for a government, an insurance company and/or an employer and presumably for the patient as well, the covenantal relationship is compromised.

Conflict between roles: the doctor, the individual patient and society

The doctor in today's society finds it increasingly difficult to differentiate his/her role and responsibilities as the agent of the patient from that as an agent of society. The conflict between these roles occurs in many aspects of practice. It is particularly evident in laws requiring that confidentiality be breached by reporting child abuse, threats of harm to another individual, or certain illnesses, such as sexually transmitted diseases, to appropriate authorities. Protecting the confidentiality of doctor–patient relationships runs counter to social concern about the public good in these situations, and confidentiality may not be upheld as an overriding ethical principle (Freudenheim, 1991).

There are many potential repercussions of compromising confidentiality, including the possibility that patients will no longer trust their doctors with certain types of information or seek appropriate or necessary care. These issues have been raised most often around the requirement to report HIV positive individuals in order to trace contacts and advise them about risks, or in reporting patients who have made threats of violence, or who have committed child abuse or crimes of violence.

Another aspect of these conflicting roles, with important ethical considerations, includes pressure on doctors to make decisions based on non-clinical indications. For example, for economic reasons such as increasing the reimbursement to a hospital, a doctor may be pressured to recommend a certain treatment or to admit or discharge a patient when, in his/her clinical judgement, this is not the best approach. Doctors may also be asked to take responsibility for treatments they have not personally recommended or administered because other personnel, who may not be legally qualified, have been the direct caretaker of the patient. This request places the doctor in an ethical (and legal) dilemma and potentially harms the patient, often without his/her knowledge or consent (Nadelson, 1986). In the US these practices affect women patients more than men because women use health-care facilities more often, and are more likely to be poor, and treated by a number of different kinds of health-care providers (US National Institutes of Health, 1990).

Paternalism and informed consent

Historically, the organisation of health-care delivery was hierarchically based, with the doctor dominating the system. The expectation that the doctor, who in the past was usually male, was informed, authoritative and protective conformed with traditional social roles of women and men (Notman & Nadelson, 1978). Although the numbers of women doctors have increased, their relative absence from policy-making positions essentially preserves this traditional type of paternalistic perspective.

In many instances, decisions about an individual patient's care, or policy about resource use and priorities have been based on this perspective, so that the best interests of the patient may be determined by others, often with little input (Nadelson & Notman, 1979, 1990). In the US this is best exemplified in policies related to reproduction, including availability of sterilisation or abortion, and allocation of resources for new technologies, like *in-vitro* fertilisation. A recent decision in the US to prohibit the use of RU 486, an abortifacient that appears to have other possible medical uses, is a specific example. Among the potential uses are treatment of some types of breast cancer, brain tumours, Cushing's Syndrome and endometriosis (Wickenden, 1990). The decision was based on the values and beliefs of those with decision-making authority, not those who would be most affected. The potential benefit of the other uses was not seriously weighed. Another example was the recent judicial ruling that ordered a woman convicted of child abuse to have an implanted birth-control device as a condition for her probation (Lewin, 1991). These decisions have raised serious ethical and legal debate, which has not yet been resolved.

Recent discussion about medical and surgical care including the performances of transplants and bypass surgery suggests that bias exists regarding criteria for the choice of suitable patients. Women and minority-group patients are less frequently offered these options in the US (US National Institutes of Health, 1990; Abraham, 1991). The documentation of gender bias in medical care and in research has led to the creation of an Office of Research on Women's Health by the United States government and to proposed legislation to address the "inadequacies in the treatment of women's health in three critical areas: research on women's health, access to services, and prevention activities . . ." (US National Institutes of Health, 1990; Markey 1990; Palca, 1990).

The negative aspects of paternalism are also seen in research policy, exemplified by banning the use of foetal tissue for research. This was done because it was felt that more women would seek abortions if they felt there was a justification, or that 'good' use could be made of the products of conception. Not only is this supposition unsupported by data, but it reflects a patronising and paternalistic view of women. The decision was made by government officials, based more on political pressure than ethical principles (Boston Globe, 1991; Hilts, 1991).

Failure to include those affected by decisions in the decision-making process, is an aspect of paternalism. At the same time, while there has been an increase in paternalism in the US health-care system (exemplified by the encroachment by government and insurance companies on policies involving medical care) there has been a decrease in paternalism in the individual doctor–patient relationship. Patient expectations that they be informed and participate in decision-making regarding their own health care have affected this relationship and the locus of decision making has shifted towards the patient and family, at least when it is not in the hands of the government or insurance companies. A recent article stated that in the past, doctors "were empowered to make health care decisions for the benefit of the patient because they understood that patient's condition better than any layperson. Now . . . the physician's role primarily is to explain the various options of treament – the pros and cons. The physician is the adviser, not the decision-maker" (Scheier, 1991).

Paternalism, then, has shifted away from the doctor into the hands of bureaucracies. This confuses the picture for patients who do not know who to turn to or blame, and intensifies discontent with the lack of responsiveness of the system. This is particularly important because of what we know about an individual's illness and his/her expectations of those who are caretakers and healers.

Illness engenders responses that may be at variance with an individual's usual behaviour, especially since those who are ill become more dependent on others. The patient who perceives him/herself as needing to be cared for by a strong, parental figure can become too compliant. At times of crisis and in gratitude for being helped, the patient may also surrender aspects of his/her autonomy (Notman & Nadelson, 1978). Ethical questions can be raised when the patient is encouraged or required to be passive and thus may not make an informed decision (Kahana & Bibring, 1964). These patient responses may further encourage the physician or the bureaucracy to maintain greater authority than may be in the best interest of the patient. This can prevent communication and the development of mutual respect between doctor and patient, and can lead to disappointment, antagonism, and mistrust of the system and those providing care in it (Notman & Nadelson, 1978).

One way of dealing with these reactions in patients has been to compel the doctor or the health-providing agency to detail, in advance, the dangers and risks of a particular procedure or medication. Despite these efforts, however, we know that barriers to communication arise from the nature of the relationship itself. An official recommendation, whether explicit or implicit, can overshadow a cautionary statement. The language may not be understood and the implications not heard, or they may be so frightening to the patient that in order to agree, he/she must ignore potential problems or complications. Thus, the authority of a doctor or institution may prevent a patient from objectively assessing dangers, benefits, or alternatives, even if they are clearly stated. On the other hand, a patient may also compromise his/her care by developing a negative response to a paternalistic posture and being mistrustful and unwilling to accept advice or recommendations, or by over-reacting to a statement about risks and side-effects (Notman & Nadelson, 1978). These responses raise questions about how we understand and obtain informed consent from patients.

Since informed consent implies understanding and assent, a patient's inability to comprehend the language used by the doctor, the insurer, or other health-providing agencies due to educational level, mental illness, or other factors, can be seen as violating the principle of obtaining informed consent (Applebaum & Grisso, 1988). Thus, those in authority influence the patient's perception of his/her options and alternatives, and affect compliance and decision making (Nadelson & Notman, 1979).

As in treatment, the agreement to participate in research may be influenced by a subject's perception of the experimenter as possessing superior knowledge and authority. Agreement may be given by a person who appears to be willing, but may not be able to make an objective decision (Nadelson & Notman, 1979). Obviously, it is not possible to change the nature of the relationship entirely or perhaps even substantially, but every effort should be made to prevent distortion and promote mutual participation.

In the research area, an often-quoted example of ethically unacceptable research was a study on contraception in Mexican-American women (Katz, 1972). One group of women was given contraceptive pills and another was given placebo and a vaginal cream, known to be a less effective contraceptive. All of the women believed they were protected from pregnancy. The misuse of the trust of the subjects was deceitful; the subjects never gave informed consent and the women were unknowingly exposed to the risk of pregnancy. Just as it exists between a doctor and a patient, the importance of a partnership built on mutual trust exists between a researcher and a subject (Nadelson & Notman, 1979). The subject must understand the information given and make an informed choice to volunteer.

Autonomy and reproduction

The special characteristics of women's reproductive roles lead to specific ethical considerations. Since decisions about childbearing, contraception, abortion, sterilisation and surgery involving reproductive organs have profound social consequences, the autonomy of a woman in deciding these questions is often challenged. From a historical perspective, debate about contraception and abortion have escalated when there are desires for population expansion (Nadelson & Notman, 1979).

In most cultures, women have generally not been in a position to achieve their own goals if they are distinct from those of their family and society. Decisions about medical care or surgical procedures that have an impact on sexuality and childbearing are often made by others, including governments and families. For example, whether sterilisation or abortion is funded can determine if a woman can make that choice. Decisions may reflect the personal, cultural or religious values of the doctor, the family, or society. A father may insist that his pregnant teenage daughter cannot have an abortion because he does not believe in it, or a gynaecologist may assume that a woman past 40 would want a hysterectomy or sterilisation because she would not want to expose herself to the risk of having a defective child. In these cases, the actions taken or assumptions made can compromise the woman's autonomy.

A recent, troubling ethical dilemma has involved genetic testing in pregnancy. When used to diagnose genetic disorders, it may lead to a decision to have an abortion. Many believe that abortion should not be performed for any reason, but even those who do not share this view are troubled by the potential use of abortion for social reasons including family finances, unmarried status or even sex selection. From an ethical perspective any restriction can be said to limit a woman's autonomy, and to place the interests of the mother in opposition to those of the foetus. When can they be considered equal persons? The question of determining when 'personhood' can be said to exist is an important consideration in this ethical debate.

Since genetic testing using amniocentesis or sampling of chorionic villi can also reveal the sex of the child, an abortion could take place if the baby were not of the desired sex. In those families and cultures where boys are more valued than girls, this could result in major changes in population demographics. The argument has also been made that once these new technologies are available, control of their use is not possible. Thus, unethical or coercive practices could result, including forced abortion.

As society and medicine change, the doctor must become accustomed to a range of new realities. These include the extensive use of reproductive technologies, the possibility of sexually transmitted disease in a wide diversity of patients, and requests for artificial insemination for unmarried women and homosexual couples (Notman & Nadelson, 1978; Stotland, 1990). As I have suggested, the emergence of AIDS in all segments of our society has also raised ethical considerations regarding testing, the right to privacy and protection of others.

The use of *in-vitro* fertilisation, artificial insemination by donor and surrogate motherhood have also stimulated ethical debate and legal action. The new technologies "raise the specter of reproduction totally controlled by females whose uteri, despite methods of laboratory fertilization, remain essential for growing fertilized ova to human status. Patriarchal dominance and male lineage are suddenly at risk. Affiliative rights and knowledge of parenthood, particularly of fatherhood as an aspect of identity, become unsure. Even the social mother can no longer state with certainty that this is her biological offspring" (Brody, 1988).

These techniques and their use raise questions about the role of biological versus social parents, the rights of children born from these procedures, and the nature of informed consent by all parties. A woman making a surrogate contract, for example, may have been coerced, or she may not be able to make an informed decision because she cannot predict her feelings after gestation. The advent of surrogacy has also brought into focus questions about whether women can be used as incubators and whether foetuses have become commodities, raising the spectre of forced pregnancy presented by Atwood (1986) in *The Handmaid's Tale*. Certainly, contractual surrogacy places pressure on poor women to rent their bodies.

An aspect of the use of emerging technology that is especially salient for psychiatrists is the expectation that they can predict outcomes and psychological risks of surrogacy despite the absence of data on psychological impact. Not only is information lacking on how those involved in surrogacy will fare, but there are no data on the outcome for children born into these families. There are also no guidelines or criteria for selection of surrogate mothers and families. Currently, arrangements are made by entrepreneurs with minimal ethical or legal constraints.

Debate about this subject has been polarised and no clear principle or policies have been formulated. One recently articulated perspective that has attracted attention is that relationships, not genes, should determine parental rights and responsibilities (Rothman, 1989). Rothman believes that gestational mothers, with nine months of relationship before the birth of their babies, should have more rights than do fathers or adoptive parents. The priority she proposes would change as fathers or adoptive parents develop nurturing relationships with these babies.

Additional ethical questions involving the rights and status of children born through these new techniques remain unsettled. The right to know one's genetic, family and medical background has been controversial in cases of adoption; certainly it is in cases of surrogacy or artificial insemination. There is a potential conflict between the interests of the 'parents' in privacy and the right of the child to know.

Techniques which allow embryo freezing with potential for later use raise additional ethical dilemmas when couples divorce or die, or when they seek to terminate the 'life' of the embryo. A new kind of paternalism also arises when procedures and technologies are reserved for specific types of individuals or situations, for example, *in-vitro* fertilisation only where there is an organic impediment to conception, or when the women are married heterosexuals (Van Hall, 1988).

Substance abuse during pregnancy has been another subject of recent ethical and legal controversy. In the past, the foetus was viewed as a potential threat to the mother's life and health, since pregnancy and childbirth had substantial morbidity and mortality rates. In recent years this view has shifted so that mothers are seen as potential threats to their offspring, and not necessarily acting in their best interests. This change in perspective has led to legal action and even prison sentences for pregnant alcoholics and addicts. This pits the autonomy of the mother against the interests of the foetus. In addition, it has changed the nature of the obstetrician–patient relationship. In this situation, when the obstetrician is treating both the mother and foetus as 'the patient', the mother's autonomy can be compromised. The foetus is accorded both rights and 'personhood', as is the mother. They obviously cannot be entirely equal, bringing into question, as suggested above, when and whether the 'personhood' of the foetus can be differentiated from that of the mother (Bowes & Selgestad, 1981; Lenow, 1983; Blank, 1986; Johnsen, 1987; Landwirth, 1987; Murray, 1987; Rhoden, 1987; McNulty, 1987–88; Cole 1990; Harrison, 1990).

Another controversy involving pregnant women concerns consent for *in-utero* treatment of their foetuses, and whether failure to consent constitutes foetal abuse. Here a distinction between moral and legal responsibilities of the mother has been made. It is generally held that a pregnant woman cannot be coerced to accept treatment to benefit her foetus. The doctor's ethical duty according to the American Medical Association (1990) is to be non-coercive and accept the informed consent of the patient.

Doctor–patient sexual interaction

An issue of increasing concern in the US today is sexual interaction between doctor and patient (American Medical Association, 1990). Because of the intimate nature of the doctor–patient relationship, a wide range of emotions, including sexual feelings, are evoked and there is a potential for overt sexualisation of the interaction (Gabbard, 1989). The incidence of sexual contact between doctors and patients is difficult to document, but those studies that have been done, coupled with recurring ethics complaints and lawsuits, suggest that it is not an infrequent occurrence (McCartney, 1966; Shepard, 1971; Kardener, 1974; Perry, 1976; Holroyd & Brodsky, 1977; Romeo, 1978; Gartrell *et al*, 1986; Derosis *et al*, 1987; Rapp, 1987).

Between 5 and 10% of psychiatrists and psychologists have reported sexual contact with patients. Although there have been recent reports suggesting that the incidence of sexual contact is decreasing, it is not clear whether this reflects an actual decrease or a change in reporting patterns. There are no specific data available on sexual interaction between patients and non-psychiatric doctors, but one study suggested that the figures may be comparable (Kardener *et al*, 1976). For psychiatrists in the US, it has been estimated that about 88% of reported incidents of sexual misconduct involve male psychiatrists and female patients; 7.6% involve male psychiatrists and male patients; and 3.5% involve female psychiatrists and female patients (Gartrell *et al*, 1989; Simon, 1989).

Desires for secrecy and the patient's dependency on the doctor to protect their confidentiality complicate our ability to learn of this problem or to intervene (Marmor, 1976; Dahlberg, 1970). Many women fear being publicly exposed, especially if they have participated in a long-term sexual liaison, or they feel betrayed or demeaned and do not want public acknowledgement of their activities (Nadelson, 1989).

Doctors become sexually involved with their patients for a variety of reasons. Women may appear to be seductive to the doctor who, due to depression, loneliness, disappointment, or stress, may be particularly vulnerable to being needed or sexually desired. These problems may lead him to respond sexually to a patient who enhances his feelings of importance and effectiveness, or who is physically appealing. Some doctors who become involved in this behaviour are sociopathic or compromised by alcoholism or substance abuse. Although a patient may misinterpret 'warmth' and physical contact, such as hugging, by a doctor as sexual, when it is not so intended, it remains the doctor's responsibility to be clear about the boundaries of the relationship (Nadelson, 1989).

Given the nature of the transference in the doctor–patient relationship, the patient's ability to give informed consent has been questioned (Kardener, 1974; Herman *et al*, 1987; Kluft, 1989). The analogy to rape and incest has been made by many clinicians (Gabbard, 1989). This is especially related to the transference aspects of the therapeutic interaction (Barnhouse, 1978). In some states in the US there are specific laws based on these special characteristics. Since 1985, sex with patients has been made a felony in seven states, and others are moving in this direction (Goleman, 1990).

Although some doctors have claimed that the sexual interaction is 'therapeutic' despite evidence to the contrary, it has been explicitly stated to be unethical and exploitative by the American Psychiatric Association (1989) and the American Medical Association (1990). The ability of the doctor to be objective and to give necessary care is compromised by breaching the therapeutic boundary. There are times when the nature of the therapeutic relationship is not clear, for example, the doctor who has consulted briefly on a patient, or has provided care that does not involve intense interpersonal relationship. Likewise, questions have been raised about when a patient ceases to be a patient and how long one can assume that the transference would be operative.

A number of clinical studies have stated that sexual relationships between carers and patients are harmful to patients and may have acute as well as long-term consequences (Burgess, 1981; Bohoutsos *et al*, 1983; Feldman-Summers & Jones, 1984; Pope & Bohoutsos, 1986; Herman *et al*, 1987; Kluft, 1989). In addition to the shame, guilt and mistrust they experience, these patients have been reported to suffer from post-traumatic stress disorder, anxiety and depressive disorders, sexual symptoms, sleep disorders, and are at higher risk for substance abuse. There have also been reports of increased suicide risk and psychiatric hospital admission.

Conclusion

This paper has briefly touched on some contemporary and emerging ethical issues, including those that especially affect women. For the doctor, the complex dynamics of his/her relationship with the patient demand constant vigilance in order to be clear about his/her role as the patient's advocate as opposed to the agent of society, and the special nature of the boundary of professional and personal relationships. For society, the changing role of women and the emergence of new technologies, especially those involving reproduction, have raised questions with profound ethical implications. It is also clear that culturally determined values and ethical values may clash. It appears at the moment that there is no consistency to medical decision-making or a process for resolution. Perhaps the way forward lies in continued discussion, education and mutual understanding.

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Issues for Women in the Development of Mental Health Services

FIONA SUBOTSKY

"Except as occasional consultants, the less men doctors have to do with female lunatics the better". (Lowe, 1883)

"As long as women are over-represented among mental patients and family caretakers and under-represented among psychiatrists, administrators and politicians, their lives will continue to be unhappily affected by decisions in which they take no part". (Showalter, 1987)

As in other health authorities, we have been involved over the last few years in developing plans for psychiatric services – driven particularly by the need to find alternatives to long-term institutional care, and also, in Camberwell, by the intended integration of two neighbouring 'providers of mental health care'. Many meetings were held and papers written on the services for in-patients, out-patients, day patients, children, the elderly and so forth, the basic required approach being to test the provision against various principles of good practice. However, none of this generated any attention to the specific needs of women. How could this be remedied?

In this paper I decribe our first attempts to establish principles for good mental health services of relevance to women, and to consider them in relation to the current local services, using a woman's life-cycle approach.

Developing principles

Women's views can be sought and brought into the planning process from a variety of levels, as in the examples below.

(a) Historical overview

The two classic, avowedly feminist, texts in this field are Phyllis Chesler's *Women and Madness* (1972) and Elaine Showalter's *Women, Madness and English Culture, 1830–1980* (1987) both of which consider the 'equivalence' of madness and femininity, adducing many examples of this process at work, and describe fashions in the presentation of women's symptoms and in the (usually) male medical response. Both conclude that women must have power within the institutions and speak for themselves rather than be spoken for.

(b) National and 'expert'

A report from the Women's National Commission (1988), *Stress and Addiction among Women*, particularly recommended:

(i) more training on stress management and improving working conditions to reduce stress on employees, including parents with young children

(ii) district health authorities and social services departments should support and help to fund administration of voluntary groups which are contributing positively to the prevention of stress among women and to education in handling stress, including parent support groups

(iii) in undergraduate and postgraduate medical education, attention should be brought to the reality of the stress caused by pre-menstrual tension and post-natal depression and to the need for early recognition of symptoms and prompt application of effective treatment

(iv) counselling should always be available for those under stress of bereavement, including losses such as miscarriage and stillbirth; pre- and post-operative counselling should be available for those undergoing hysterectomy, mastectomy and abortion

(v) the role of health visitors and school nurses should be recognised and supported.

Ashurst & Hall (1989), consultant psychotherapists drawing upon their experience "as women, wives, mothers and doctors", suggest, "The way to help a woman with physical or mental symptoms due to emotional causes is by understanding her predicament in terms of her image of herself as a woman, particularly in terms of her reproductive function, and by tracing her story back to the key events that precipitated her distress".

(c) Local service professionals

Using the equal-opportunities policy of the health authority as a way of looking at existing services has, in Camberwell, begun to raise issues concerning women through the mechanism of an "equal opportunities implementation group" and two quality circles to address women's issues and black and ethnic issues. So far the women's issues quality circle has emphasised the need for:

(i) liaison between psychiatry and obstetrics/gynaecology
(ii) availability of female staff for women patients
(iii) better access for push-chairs and wheelchairs
(iv) the development of specialised services
(v) better information about resources
(vi) attention to safety issues for women staff
(vii) more women in senior staff positions.

(d) Local service users

A group set up to consult with women users of in-patient services revealed concerns about:

(i) violence and sexual harassment on the wards
(ii) not enough private washing and bathing facilities for female patients
(iii) general lack of privacy for women
(iv) the need for a mixed staff group.

(e) Local outside forum

Other ideas have emerged through the recent development of an interested local group in Camberwell, the Southwark Women and Mental Health Forum:

(i) childcare for users and visitors
(ii) 'women-only' space
(iii) access to women staff
(iv) access to community languages
(v) training for staff in issues concerning child sexual abuse, sexual abuse and equal opportunities
(vi) low-cost counselling
(vii) befriending, advocacy
(viii) consumer involvement.

Services through the life-cycle

Childhood

Services involved with children's mental health are not confined to child psychiatry, but include the general and specialist aspects of education, social services work, primary health care and paediatrics. For an inner-city area the deprivation factors for children are known to be high and are reflected in the high numbers of children on the child protection register, the high infant mortality rate (Camberwell Health District Department of Public Health, 1989) and the high rate of childhood disturbance (Rutter *et al*, 1975).

Within this high level of need, girls have not usually been considered separately, although there is evidence of differential provision of service. Annual reports show that the local child psychiatric services tend to see more boys than girls (ratio of about 2:1), with a slightly decreased ratio for the hospital clinics in comparison with the community clinics. These rates have been very consistent over the years, despite considerable alterations in some referral patterns, and despite the increased awareness of child sexual abuse, which might have been expected markedly to increase referrals of girls. However, the proportion of girls was higher when a child psychiatric session was provided within a primary health care setting and from links made with the voluntary agency Victim Support, so there might be a value in developing and circulating information about specialised services for girls.

Child psychiatric assessments for special education are requested less commonly for girls (Subotsky, 1990) and the special education facilities available for emotionally and behaviourally disturbed children are so predominantly occupied by boys that the environment is unsuitable for girls. The major reasons for this sex difference are evidently to do with 'troublesomeness' rather than other criteria for disturbance or distress, and reading difficulties are often associated, which are less common in girls.

An improved information system would enable systematic evaluation of the use of resources for girls – is more, or less psychotherapy provided, are outcomes different?

Adolescence

Both adult and child psychiatry services are involved with two particular types of serious problems of adolescence where young women present more often than young men – eating disorders and self-harm. Anorexia nervosa is a life-threatening disorder, for which considerable and expert intervention is necessary; fortunately it is well recognised and the appropriate expertise and back-up of in-patient beds are usually readily available.

Self-harm, or parasuicide, presents through the hospital accident and emergency department and both the adult and children's psychiatric services are able to respond readily, being based within the hospital and having well organised systems of multi-disciplinary response. Methods of intervention need continued development, as the risk of further self-harm and/or depression is clear, but the failure rate for follow-up is high. It is now thought that sexual abuse may be an important predisposing factor in both self-harm and anorexia nervosa. It is therefore important for all staff to receive adequate training in order to be able to elicit this type of history and intervene appropriately.

Menstruation and fertility

Psychological problems surrounding menstruation, especially pre-menstrual tension, are largely dealt with by general practitioners, with only occasional referral to specialists, whether gynaecologists or psychiatrists. However, effective treatment is not yet standardised (Gath & Iles, 1988) and there has been little formal trial of psychological treatment, a situation compounded by definition problems.

Camberwell has a higher fertility rate, abortion rate and birth rate than the regional and national averages, suggesting that although there are family-planning services these are not effectively reaching girls and women; this might well be one of the key preventive areas for women's mental health. Infertility can also be a source of major stress, and the development of 'high-tech' methods of investigation and treatment, especially when unsuccessful, could be expected to add to this.

Sexual relationships, marriage and separation

Women's experiences of difficulties with their sexual relationships range from communication problems to severe physical and sexual abuse, which increase their vulnerability to psychiatric disorder (Mullen *et al*, 1988). Facilities for these sorts of problems include voluntary agencies such as Relate, Victim Support, Women's Refuges, and psychosexual and marital therapy in the hospitals. However, liaison with the mainstream psychiatric services could be improved, and further specific services for treating the aftermath of abuse are needed.

Pregnancy and its loss

Counselling is generally available in association with termination, especially for younger women through teenage pregnancy clinics, and there are well developed multidisciplinary psychological and psychiatric liaison services to obstetrics and gynaecology. Nevertheless, clinical experience indicates that single and repeated losses through termination, miscarriage or stillbirth may have effects on a woman's emotional adjustment over many years, and the development of policies of good practice such as suggested by Savage (1988) for the management of perinatal death could be useful. Support groups such as the Miscarriage Association and the Stillbirth & Neonatal Death Association are valuable, but are they accessible to the ordinary local population?

Child-birth and post-partum

'Baby blues' are well known to midwives, health visitors and district nurses, who effectively deal with most early problems of motherhood and should have good liaison and training links with the more specialised services. Severe post-natal mental illness occurs in about 1 in 600 pregnancies and needs urgent and intensive intervention; fortunately there are specialist services available, with in-patient back-up, but extra community nursing support would enable more women to stay safely in their own homes while ill (Oates, 1988).

Motherhood

Women's experience of psychological distress as mothers, especially of young or handicapped children, is likely to be recognised particularly by the primary health care, paediatric and child psychiatry services. The importance of this is underlined by Brown & Harris' major study *Social Origins of Depression* (1978) which was carried out in inner London and revealed four major factors leading to "the provocation and generalisation of hopelessness":

(a) the loss of the mother to a child under 11 years
(b) lack of an intimate confiding marital relationship
(c) lack of paid employment outside the home
(d) three or more children under 14 years.

It has been estimated that depression in mothers of young children in the inner city may be as high as 30–40% (Wolkind, 1985) and this can have an impact on the children (Pound *et al*, 1988), leading to a vicious circle of family stress. Single parenthood is very common in inner cities. Developing and supporting voluntary services and self-help groups may be one of the most effective interventions from the health service, and there are a number of useful agencies, including the Family Service Unit, the Family Welfare Association, Welcare and Newpin.

Middle age and the doctors

Body and mind connections surround much hospital involvement of women in their middle life, even though classic 'hysterical' symptoms are now rare. For instance, a gynaecologist comments "the greatest challenge to the clinician is establishing whether psychological disturbances are due to oestrogen deficiency or result from coincidental but concurrent socio-domestic-economic crises" (Whitehead, 1983); hysterectomy is "not likely to lead to adverse psychiatric sequelae in patients who are psychiatrically healthy before the operation" (Osborn & Gath, 1983), while on the other hand mastectomy "is predictive of a depressive state" (Deadman *et al*, 1989). Obviously, much will depend on the meanings and values ascribed to the menopause, hysterectomy and mastectomy by individual women, as well as the resultant alterations of physical state. Perhaps just as male 'shell-shock' provided a model of psychologically caused disturbance to legitimise female 'hysteria' (Showalter, 1987), so will 'post-traumatic stress disorder', another special diagnosis for male soldiers, promote the acknowledgement of severe perceived stress in women's lives as causal in their distress/disturbance and encourage the further development of effective treatment. Meanwhile, most hospitals do have mastectomy counsellors, with active psychiatric services to obstetrics and gynaecology departments, and there is research into many aspects of psychosomatic disorder. The hospital social workers also provide a crucial contribution to the relief of emotional, social and family stress.

Women and the general psychiatric service

Women frequently consult general practitioners for psychological problems and, at least in the past, were quite likely to be prescribed minor tranquillisers with the risk of later dependency. A greater use of non-medical counselling as well as of specialist resources in primary health care rather than hospital out-patient departments would have the advantages of accessibility, less stigma for the patients and greater continuity of care (Tyrer, 1984).

As 'acute' bed provision has declined, the remaining in-patient beds have altered in their use, with a higher turnover of a younger and more disturbed population (Patrick *et al*, 1989). Since the wards within Camberwell are admittedly cramped and old-fashioned, with few single rooms, it is not always easy to safeguard vulnerable patients from those with a tendency to 'act out'. The incidence of sexual harassment and even assault has become a major issue, although of course very difficult to gather accurate information about. It has been helpful to understand that this is a general risk in institutions caring for vulnerable people. Initial policies to promote patients' safety have been worked out following consultation with staff, patients and community groups. The "Statement on abuse and harrassment" from the Royal College of Psychiatrists (Gath, 1989) has been useful, as has *Thinking the Unthinkable* (Brown & Craft, 1989) but it is clear that there are major training needs for staff in this area and that enabling women patients to speak out effectively, perhaps with advocacy services, would be an advantage.

Within inner London, some funding has been available for voluntary groups and it has been possible to provide financial support from the psychiatrist budget towards a women's befriending scheme, a local MIND advice and information scheme and the Lambeth Mental Health Forum, all of which are available for informal access and can provide important feedback on the quality of services for women.

The appropriateness of services for ethnic minority women, especially those of Afro-Caribbean origin, remains largely unknown, and needs urgent evaluation. In Camberwell, links with the Afro-Caribbean Mental Health Association are fostered and a specialist community mental health team has been set up, but much remains to be done. It is unfortunate that 'Shanti', a counselling service for ethnic minority women in a neighbouring health authority, is currently at risk owing to lack of funds.

Old age and its care

Alzheimer's disease affects women disproportionately as sufferers, because of their greater life expectancy, and as carers. Gilleard *et al* (1984) have shown that emotional disturbance is common among the 'supporters' of the elderly mentally infirm, especially women, but there is some evidence (Gilhooly, 1984) that community provision can help to relieve the distress. The psychiatric services for in-patient and community care for the elderly severely mentally infirm are generally well co-ordinated and do provide support for carers. In contrast, the in-patient environment can be extremely unsuitable. In Camberwell these facilities need urgent replacement; there is also a considerable shortage of day places. For women over 65 there is a particularly high risk of suicide and self-inflicted injury (standard mortality rate = 195, England and Wales 1986 = 100; Camberwell Health District Department of Public Health, 1989), which underlines the necessity for continued pressure to separate in-patient provision for the 'elderly functionally ill' from younger patients.

Countrywide there is a need for good collaboration between the elderly services and voluntary groups such as the Alzheimer's Disease Society and Age Concern.

The service providers

Nationally, there are more women in psychiatry at a senior level than in many other medical specialities (Medical Manpower and Education Division, 1989), despite Henry Maudsley's (1874) view that, as woman's mental and physical organisation was inferior to that of man's, she should be prevented from taking up a career, particularly medicine. Indeed, staff in most of the mental health professions are mixed, so that specific access to women for women should be possible if wished. Both women and men, however, have undergone the same educational experiences and work in the same system, in which equal-opportunities policies may only receive bare compliance, so that a more 'woman-orientated service' does not automatically follow, unless specifically fostered, and women may continue disproportionately in the lower career grades.

Conclusion

Whether or not one agrees with Hilary Allen's (1986) view that "deeply ingrained sexism characterises much psychiatric practice", as she also says, a reformist rather than a revolutionary approach may be more constructive. From the above exercise it is clear that improving and extending the processes of consultation about women's needs and wishes is more important than finalising conclusions at present. Two clear themes emerge: the importance of lessons learned from growing knowledge about sexual abuse, especially listening to and believing the victim; and the importance of the role of the consumer, as patient or carer, in influencing the health services received. All those involved in drawing up the new 'service specifications' please note.

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Depression in Women

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Depression in treated samples shows an approximately 2 : 1 female predominance. The sex ratio is not due simply to more help-seeking behaviour in women, for it applies equally in studies of community prevalence. Differential acknowledgement and direction of distress may be a partial explanation, supported by male predominance of alcoholism and completed suicide, and by a possible recent increase in depression in young men. Biological mechanisms acting through hormonal effects on the brain are plausible, but hard to test. Epidemiological studies indicate that much of the excess occurs in married women aged 25–45 years with children. This strongly suggests social causation and highlights the vulnerable situation of young mothers. The full explanations for the sex difference are not yet clear, but are likely to combine factors related to expression of distress, biology and social situation.

Depression is the most prevalent disorder in psychiatry. It is also a condition in which illness shades imperceptibly through subclinical distress to a normal mood which is part of universal human experience. Defining thresholds for the disorder and trying to think separately about disorder and normal mood has therefore been important, even if abrupt distinctions are artificial. Community prevalence studies indicate that 5% of the population satisfy the criteria of the Present State Examination (PSE; Wing *et al*, 1974) or DSM-III (American Psychiatric Association, 1980) criteria for defined psychiatric depression in a six month period.

Perhaps the most striking fact about depression is its differential sex incidence, with more women affected than men. This paper examines in detail the differential sex ratio and considers alternative explanations for it. It is not possible to point to one single explanation, or indeed to many firm conclusions, but in my view the evidence is gradually making up a consistent story.

Sex ratios

Table 1 shows sex ratios in treated cases of depression in some representative studies in Western cultures between 1942 and 1973, reviewed by Weissman & Klerman (1977). There are many other studies, and more recent ones, but they also show a female predominance. The average female : male ratio in these studies was around 2.1 : 1 and all showed female predominance. In the literature as a whole there are some exceptions, but not many.

A number of broad explanations for this difference have been advanced. The first suggests that perhaps it is entirely an artefact: women may simply seek help more for the depression which both sexes have equally. A second obvious set of explanations has to do with biological make-up: there may be genetic differences due to the different chromosomal make-up of the sexes, or female sex hormones may have an effect in some way. A more popular line of explanation lies in social effects of life stress, of social vulnerability factors and absence of support, and of women's role in society more widely. A fourth explanation is that the two sexes may differ in the way distress gets acknowledged and directed: into depression in females, in other ways and disorders in males. This explanation lies somewhere between and involves aspects of all the other three.

Table 1
Sex ratios in some studies of treated depression (from Weissman & Kerman, 1977)

Study	female : male ratio
USA	
Cooper *et al*, 1942	2.0
Wechsler, 1961	2.6
Gardner *et al*, 1963	2.1
Rosen *et al*, 1964	1.6
Duvall *et al*, 1966	2.3
Tarnower & Humphries, 1969	2.4
Lehmann, 1971	1.7
Paykel *et al*, 1970	3.0
Pederson *et al*, 1972	1.5
Cannon & Redick, 1973	2.1
Europe	
Kielholz, 1959	1.6
Essen-Moller & Hagnell, 1961	1.8
Juel-Nielsen *et al*, 1961	3.0
Odegaard, 1961	1.4
Adelstein *et al*, 1964	1.9
Grewel, 1967	2.6
Lehmann, 1971 (England)	1.6–1.9
Mean	.2.1

The remainder of this paper will examine detailed evidence for each of these broad explanatory hypotheses.

Help-seeking behaviour

Conclusive answers from the literature can only be given to the first explanation: the differential sex ratio is not simply due to differences in help-seeking behaviour. There are some well documented differences in the extent to which the two sexes tend to use medical services in general. Most studies of attendance at doctors for physical or psychiatric complaints, show women attending more. For instance, Hinkle *et al* (1960), in their study of telephone employees in New York aged over 20 years, found women had more visits to the doctor and were away from work for health reasons more frequently than men. These differences were almost all accounted for by minor illnesses: men had more life-threatening illnesses and had higher death rates. Higher consulting rates do not necessarily mean a greater readiness to consult: they might simply mean more illness. Kessler *et al* (1981) analysed data for psychiatric symptoms from four large-scale community surveys. Women did report more psychiatric distress but also showed a greater readiness to consult at the same level of morbidity: this appeared to be due to a greater readiness to translate non-specific feelings of distress into a recognition that they had an emotional problem.

However, for specific depressive symptoms and anxiety the female predominance in treated samples is found to an equal or greater extent in community samples. It is useful to make a distinction in these between studies using questionnaires, which report symptoms, but not necessarily of sufficient severity to reach the level of disorder, and studies employing definitions for psychiatric disorder, which usually give lower rates.

Table 2
Sex ratios of point prevalence of depressive symptoms in some community samples (from Boyd & Weissman, 1982)

Study	Female : male ratio
Martin *et al*, 1957	2.4
Warheit *et al*, 1973	1.8
Mellinger *et al*, 1974	1.8
Blumenthal, 1975	2.7
Comstock & Helsing, 1976	
Missouri	1.4
Maryland	1.8
Weissman & Myers, 1978*a*	
1967 survey	1.3
1969 survey	1.8
Mean	1.9

Table 3
Prevalence rates for depressive disorders in recent community surveys employing psychiatric definitions for major depression – PSE/ID/CATEGO and DSM–III/RDC

	Rates per 100		
	Men	Women	Total
PSE/ID/CATEGO (1 month)			
Henderson *et al*, 1979	2.6	6.7	4.1
Bebbington *et al*, 1981	4.8	9.0	7.0
Dean *et al*, 1983		5.9	
Mavreas *et al*, 1978	4.3	10.1	7.4
DSM–III/RDC (6 month)			
Weissman & Myers, 1978*b*	3.2	5.2	4.3
Dean *et al*, 1983		7.0	
Myers *et al*, 1984	1.7	4.0	3.0
Canino *et al*, 1987	2.4	3.3	3.0
Mean	3.2	6.4	4.8

With regard to depressive symptoms, Boyd & Weissman (1982) reviewed the point prevalence in some community studies. These gave relatively high rates of 13%–20% overall. Table 2 summarises the sex ratios. From these data a mean sex ratio of 1.9 can be calculated, which is virtually the same as that for treated depression.

Studies employing psychiatric definitions give lower total rates, as might be expected from more stringent criteria. Here, the recent large-scale epidemiological studies employing DSM–III/Research Diagnostic Criteria (RDC; Spitzer *et al*, 1978) or PSE criteria, including the US Epidemiological Catchment Area (ECA) studies, provide the best evidence. Table 3 summarises six-month prevalences for major depression in some of these studies. Calculating average sex ratios gives a figure of 2.0 – again virtually identical to that for treated depression.

The female predominance of depression is therefore not an artefact of treatment seeking. In the US ECA studies, women with psychiatric disorders were a little more likely to consult a doctor than men, although, if they sought help, men were more likely to turn to a specialist. The overall difference was small, around 10%–20% (Shapiro *et al*, 1984), and this was for disorder irrespective of diagnosis. There is relatively little direct evidence specific to depression of clinical intensity as to who seeks help.

Biological causes

Given that the difference is real, what is the likely explanation? Here we are on less certain grounds regarding conclusions. Part of the problem has been the absence of tough-minded research directly aimed at resolving the questions; part is that the right kinds of studies, comparing the two sexes, are not easy.

Biological explanations have centred around genes or hormones. Regarding the former, there is clear evidence from twin studies of a genetic element in affective disorders. This is most marked for bipolar disorder but fairly clear, although less in magnitude, for unipolar psychotic depression (McGuffin & Katz, 1986). For unipolar neurotic depression, although there is also a familial element, twin studies are far less conclusive as to whether its origin is genetic or environmental. Even for bipolar disorder, the genetic evidence now suggests multiple genes rather than single ones.

If a disorder is X-linked, with a gene on the X chromosome, differential sex incidence will be found. X-linked dominant disorders will be more common in women. An X-linked recessive condition, such as haemophilia, almost solely occurs in men but can be transmitted to offspring only via women.

There is some evidence of X linkage in bipolar disorder. This evidence depended initially on linkage studies using phenotypic markers, but there are now more recent studies using markers localised to the distal portion of the long arm of the X chromosome which show X linkage (Mendlewicz *et al*, 1987). If it does occur, it is only in some families rather than in all. However, this is unlikely to explain the sex incidence. The biggest problem lies in the sex incidence of bipolar disorder, which is approximately equal. Here there are some good studies of incidence, which, where possible, is more illuminating than prevalence since it is not affected by differential prognosis. In some Danish annual incidence studies quoted by Boyd & Weissman (1982) the female : male ratios were 1.1, 1.3, 0.5, 1.3, averaging, in this unrepresentative series, at 0.9. These studies are not exhaustive but others, including prevalence figures in the American ECA studies, show similar trends. There is no good evidence for X linkage in unipolar disorders.

This difference between bipolar disorder and the other affective disorders in sex incidence is important and has not received enough comment. It reinforces the evidence that bipolar disorder is a separate disorder. It also appears more biological in origin than other forms of depression: perhaps this hints that the female predominance in unipolar disorders is more psychosocial in origin.

The more obvious biological possibility lies in the important hormonal differences between women and men, the former having exposure to oestrogens and progestogens rather than predominantly to androgens, and to cycling of gonadotrophins and sex hormones. Here it is virtually impossible to make useful direct female : male comparisons at present – such comparisons show the obvious, but in most circumstances are totally confounded by other sex and gender differences.

Indirect inferences can be attempted from some possibly hormone-related phenomena. Pre-menstrual tension appears to be a real phenomenon, which includes depression among other feelings such as tension and irritability. Occasionally women show virtually a clinical depression pre-menstrually, particularly, in my clinical experience, when relapsing into a depressive episode. Unfortunately, however, the specific hormonal change responsible for pre-menstrual tension remains obscure.

The remaining lines of evidence are rather negative. Oral contraceptives were blamed for depression at one time: studies are at best equivocal and several placebo-controlled studies do not show any increase in depressed mood (Weissman & Slaby, 1973). The effect, if present, is a small one: clinical major depression rarely appears related to use of oral contraceptives.

Childbirth is undoubtedly associated with an increase in onsets of major psychosis and hospital admissions in the first post-partum month (Kendell *et al*, 1987), and is a time of massive hormonal change. Increased onset of bipolar disorder does seem to occur at this time, but many post-partum psychoses are not affective. Recent evidence indicates that such psychoses are not related to recent life stress, making hormonal aetiology more plausible (Martin *et al*, 1989; Brockington *et al*, 1990; Dowlatshahi & Paykel, 1990).

Milder post-partum depression at the general practice or subclinical level is common, but recent studies (Cox *et al*, 1989) making comparisons with age-matched non-postpartum women suggest that rates are not very dramatically raised: depression is common in married women in the childbearing era. Such milder depression appears to be highly related to life events and social stress (Paykel *et al*, 1980; Watson *et al*, 1984; Cooper & Stein, 1989).

However, the excess of depression in women is by no means confined to the period shortly after childbirth. Onsets at this time cannot explain more than a very small proportion of the total.

The fourth possibility, the biological menopause, does not make a contribution. At least three studies have failed to show any peak in major depressive disorder at the biological menopause (Winokur, 1973; McKinley & Jeffries, 1974; Hallstrom, 1973), although psychosocial changes and life events occurring around this time in the life cycle may be important.

This leaves little solid to depend on. Nevertheless, it is hard to ignore the possible contribution of hormones. This need not be directly in adulthood. The developing male and female brains *in utero*, in the neonatal period and in infancy are exposed to different hormonal environments, resulting in such effects as later hormonal cycling. Differences in brain function related to level of emotionality or particular mood states cannot be ruled out, at least until brain function is better studied.

Social causes

Social causes have been the focus of more research. Stronger links are emerging, although the evidence is not as strong as some of the claims. Much of the research, for instance that on social vulnerability factors, has been confined to female samples. Before conclusions about their contribution to the sex ratio can be drawn, we need to have similar studies in men.

Social explanations have generally concerned life events, social support, or women's roles and status. Regarding the first, there is now a large and conclusive volume of research showing that clinical depressions are preceded by elevated rates of the more threatening classes of life events (Paykel & Cooper, 1991). Women do not appear to experience more life events than men. Studies in the community which have looked at the question suggest equal event rates, but that women react with higher symptom intensities to the same stress (Uhlenhuth & Paykel, 1973). Also the two sexes, when asked to rate the stressfulness of different events, weight them similarly (Paykel *et al*, 1971). The answer appears to lie in a greater vulnerability to the effects of life events, rather than more life-event stress. Such vulnerability might be genetic or environmental, biological or social.

Social vulnerability studies have laid particular emphasis on social support. They include the seminal studies of women by Brown and Harris (Brown & Harris, 1978; Brown & Prudo, 1981; Brown *et al*, 1986) implicating, most clearly, the absence of a confidant, and less consistently, the presence of young children at home, being of lower social class, not working, and early loss of mother. Although there has been much debate about these, the evidence from other studies seems quite good for the first two or three. For work outside the home there has been less replication, and studies suggest more complex effects. For instance, Parry (1986) found that, in the case of working-class women, working outside the home was associated with less depression where there was good social support; where there was not good support, however, it was associated with more depression. Important factors seem to be whether a woman chooses to work or is driven to it by necessity and whether it leaves no gap at home or produces a situation where problems with growing children are worsened. All these need testing in men. The available evidence suggests that not working because of unemployment is generally very bad for them.

The third set of social explanations concerns the psychosocial disadvantages of women's roles and status. Such hypotheses suggest that particularly the housewife role is associated with low social status. Social discrimination makes it difficult to achieve mastery by direct action and assertion, inequities lead to legal and economic helplessness, dependency on others, chronically low self-esteem, and low aspirations. Learned helplessness is induced, starting from childhood socialisation, self-images and expectations. Again, Brown's work has contributed in relation to depression by a recent focus on low self-esteem and its antecedents (Brown *et al*, 1986): again the way forward would also seem to lie in comparative studies of the two sexes.

Epidemiological studies

Epidemiological studies are starting to provide some answers concerning the interactions of sex with age, marital status and having children.

Jorm (1987) carried out combined analyses of a large number of studies of sex and age in depression. He looked at sex ratio with age and found a curvilinear relationship. The female predominance is absent in childhood, most marked in middle age, and weak in old age. In a complicated regression analysis looking at rates of depression rather than just ratios, there was a high rate for women in their 20s which declined slowly as they got older. The rise in rate reached its peak well after puberty in females, and the decline started well before the menopause and showed no acceleration then: these are difficult to explain on endocrine hypotheses.

For marital status there is a somewhat consistent trend, as was pointed out in the 1970s by Gove, an American sociologist (e.g. Gove & Tudor, 1973). He noted that high rates of many mental illnesses for women are particularly accounted for by married women: single women have lower rates, although for those divorced, separated and widowed, rates are often high. For men the ratio is reversed: those who are single have higher rates than those who are married. For men marriage appears to be protective, for women detrimental. This result was also found in the Camberwell survey (Bebbington *et al*, 1981), although not all studies support it (Romans-Clarkson *et al*, 1988). Bebbington (1987), reviewing first admission statistics for depression, found lower rates for the married than the single in both sexes, but again the effect was much more marked in men than in women.

With regard to age, sex and marital status, there are some old findings which have never achieved the prominence they deserve. Grad de Alarcon and colleagues set up a case register to compare services in Chichester and Salisbury, around 1960. Later, they reported specific referral rates for psychiatric treatment by age, sex, marital status and diagnosis (Grad de Alarcon *et al*, 1975). For depression there was the expected excess of women over men in middle age, and this was found for married women in particular. They also found an excess of neurotic depression for married women aged 25–44 years. There was in fact a later peak for psychotic depression, in unmarried women aged 35–65 years, but this was smaller and less convincing. Other studies, not altogether consistently, suggest similar results.

The last piece of evidence concerns having children. Gater *et al* (1989) found that first admission rates for affective psychosis for the North West Region were higher in women. Detailed breakdown of the results showed the excess was accounted for by women who had had one or more children. Marital status and parity are closely associated, but looking respectively at unmarried women with children and those married but without children, the excess appeared to be accounted for by having children. Unfortunately, these latter conclusions were of necessity based on rather low numbers. Once you have a child, of course, you have the social consequences for a long time. Bebbington *et al* (1991), using data for prevalence of minor affective illness, obtained similar findings, although in their data it was less clear whether having children rather than marital status was responsible.

These findings point in a consistent direction. There is a particular peak of depression in women aged 20–40 years who are married and have children. It is difficult to reconcile these findings with any endocrine hypothesis, easy to do so with hypotheses of social causation pointing to the particular problems of young mothers in developed Western societies, where families are nuclear and geographically mobile, extended family support is uncommon, and a woman with children is particularly dependent on the quality of relationships with her partner. In our own studies of life events and depression, marital arguments and break-up have been among the most common antecedent events (Paykel, 1974).

Differential acknowledgement and direction of distress

A final possible explanation for the differential rates lies in a difference in acknowledgement and direction of distress. It is commonplace that women in our society cry more readily than men. It is accepted as normal that a woman should weep on receiving very bad news but it is regarded as dubious for men to do so. This is usually explained as a matter of social acceptance in our culture, and undoubtedly much of it is. Some of it could be biological: higher emotionality might be a concomitant of greater sensitivity in interpersonal relationships and perceptiveness of the needs of others, something which might have biological value in differentiated childrearing.

This concerns normal mood but might carry over to pathological disorder. Some other problems are more common in men, particularly alcoholism and crime. Crime does not bear any great relationship to mood disorder, and in most cases it is not psychiatric. Alcoholism does have a relationship to mood disorder. Winokur (1979) described 'depressive-spectrum' disease in which women tend to have depression, while male family members have alcoholism and antisocial personality. It could be that men disguise their depression by drinking, or, at a deeper level, distress is directed into other disorders. Men have a higher rate of suicide than women, so perhaps the depression is there. There might be other explanations for this difference, however: more women unsuccessfully attempt suicide, and the choice of method may determine outcome, since men tend to use violent methods of high lethality, women to use less lethal overdoses.

It might therefore be that, irrespective of help seeking, women are more prepared to acknowledge their depression and to report it in surveys. Briscoe (1982) found women more willing to acknowledge feelings, both positive and negative. Angst & Dobler-Mikola (1984), in a community survey in a Zurich canton, found one-year prevalences for depression to be higher in women than men, but little difference between the sexes for prevalence in the last three months. They suggested the most likely explanation to be that men tended to forget. This seems more relevant to identification of mild cases in the community than to severe treated disorder.

A valuable approach in confirming this lies in studies of other cultures where such factors might operate differently. The Old Order Amish of

Pennsylvania, a fundamentalist religious group, are a subculture in the US who lead a 19th-century life, with strong prohibitions on drink and antisocial behaviour. They appear to have high rates of affective disorder. Among them unipolar disorder, as well as bipolar, shows an approximately equal sex incidence (Egeland & Hotstetter, 1983).

More distant cultures would be informative. Weissman & Klerman (1977) reviewed a number of studies from Guinea, India and Papua, where the Western sex ratio appeared to be reversed to a male predominance. Unfortunately they were all studies of treated samples. In many of these cultures women lead a life which is relatively enclosed in the family, and they might not have access to help-seeking to the same extent as men. More community studies are needed, and are starting to appear. Such studies will have to contend with methodological difficulties of non-Western ways of expressing depression, and also to look at factors which might change the rates, such as better extended family support.

A final piece of evidence is provided by Western temporal trends. There is suggestive evidence that reported Western rates of depression, as detected in community surveys, are increasing, particularly for young men, and that the sex ratios are becoming more equal. The ECA studies in the US have been inferred to show this (Klerman, 1988), as has a similar study in Christchurch, New Zealand (Joyce *et al*, 1990). Care is needed in interpretation: the conclusion depends on reported lifetime rates being higher in the young than would be expected from lifetime rates in the old, but the instrument, the Diagnostic Interview Schedule, may well be unreliable for lifetime recollection (Parker, 1987), and the elderly might simply forget.

More persuasively, Murphy (1986) has reviewed four community studies, two in the USA, one in Canada and one in Sweden, repeated 10–20 years apart. They showed a trend for sex ratios to equalise. There have been considerable societal changes towards less gender-role differentiation, especially in Scandinavia, which might both change the acknowledgement and the social stress. Perhaps men are starting to acknowledge their depression. Sex ratios for depression appear to be more equal in University students (Wilhelm & Parker, 1989), and Jenkins (1985) found no major sex differences in rates in civil service executive officers.

Conclusions

The explanations for a differential sex incidence of depression are still only tentative. The most plausible conclusion is that there are multiple factors at work in the same direction.

Help-seeking behaviour may make a small contribution to treated rates, but only a small one. Biological factors cannot be discounted, at least not those based more on the effects of hormonal environment on brain biology than on an abnormal gene on the X chromosome. There is a particular vulnerability to depression in married women aged 20–40 years with children. This strongly suggests a social explanation. Differential acknowledgement may also be important, and may be changing. More research is needed which, in illuminating this specific problem, is likely in addition to reveal much that is of central importance for the genesis of depression in general.

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Psychotropic-Drug Prescribing for Women

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The reasons for women in Europe and North America being prescribed over twice as many psychotropic drugs as men are complex. Psychiatric disorders such as depression and anxiety appear to be more common in women than in men, and women more commonly complain of psychological symptoms. There may be a gender bias in medical diagnosis and choice of medication. Sociological factors may also be involved, including the likelihood that women have fewer outlets than men for symptom control by activities outside the home (e.g. the social use of alcohol). Women also have special problems including pregnancy, lactation, child rearing and pre-menstrual tension. Probably, much use of psychotropic-drug use for women (and men) is inappropriate and not closely related to the symptoms or conditions for which they are prescribed. Furthermore, the chronic use of some psychotropic drugs, especially benzodiazepines, may compound the problem by inducing dependence and withdrawal symptoms.

Women, throughout Europe and North America, are prescribed about twice as many psychotropic drugs per head as men. This difference has been apparent for many years and been shown in many studies in many countries.

In this country, a survey of 133 081 patients registered with 48 general practitioners (Parish, 1971; Fig. 1) showed that about 20% of the women and 10% of the men were prescribed psychotropic drugs. The prescription rates rose with increasing age but remained in the same proportion. The percentage and sex distribution of psychotropic drugs have not altered since then, although different psychotropic drugs have become fashionable. Across the Atlantic, Greenblatt *et al* (1975) recorded psychotropic drug prescriptions (on admission) in 24 633 patients admitted to general medical and surgical wards in the Boston area. These showed a similar age and sex distribution, although psychotropic drug prescriptions were somewhat more generous than in England, with about 25% of the women and 15% of the men taking them. A similar prevalence and distribution has been shown in many other countries.

Of the 5079 (20.6%) patients on psychotropic medication in the Boston study, 68% were taking anxiolytics (benzodiazepines, meprobamate, barbiturates), 22% hypnotics/sedatives (barbiturates, benzodiazepines, glutethimide, choral derivatives), 4% antidepressants (tricyclics, monoamine oxidase inhibitors (MAOIs), lithium), and 3% each antipsychotics (phenothiazines, haloperidol, thioanthenes) and stimulants (amphetamines, other anorectics). The proportions of these drugs used in England were similar (Parish, 1971; Fig. 2).

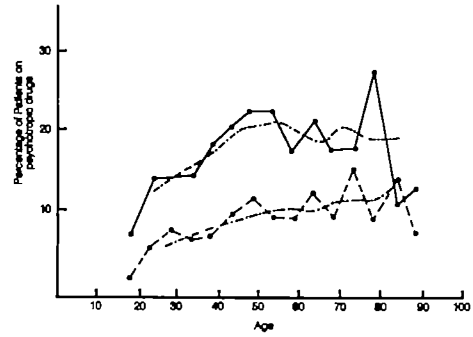

Fig. 1 Prescriptions for psychotropic drugs by age in a survey of 133 081 female (●—●) and male (●—●) patients registered with London general practitioners (-·-·-= trend line) (from Parish, 1971).

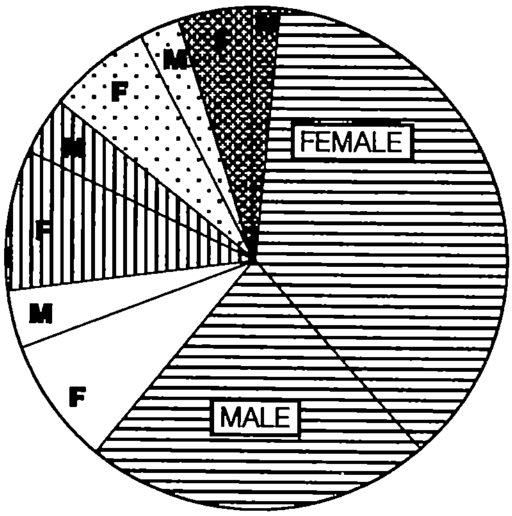

Fig. 2 Categories of drugs (▤ = tranquillisers, □ = antidepressants, ▥ = non-barbiturates, ▩ = barbiturates, ■ = stimulants and appetite suppressants) prescribed in London general practices in males (M) and females (F) (data from Parish, 1971).

Table 1
Prevalence (1980–81) of anxiolytic/sedative use (percentage of each sex using medication) in the previous year (1980–81) in selected countries (data from Balter *et al*, 1984)

Anxiolytic/sedative users	UK	Belgium	Holland	France	Germany	Switz.	Italy	USA
Men: %	6.7	12.9	5.7	11.7	8.6	10.2	9.4	8.5
Women: %	15.3	21.4	9.1	19.3	18.9	18.7	13.5	16.9
All: %	11.2	17.6	7.4	15.1	12.0	14.6	11.5	12.9
Female : male ratio	2.3	1.7	1.6	1.6	2.2	1.8	1.4	2.1

The actual numbers of prescriptions for psychotropic drugs are enormous. In the UK in 1987 there were about 25 million prescriptions for benzodiazepines (15 million hypnotics, 10 million anxiolytics), 12 million for antipsychotics and nine million for antidepressants. These figures are for a population of about 55 million and do not include barbiturates, other hypnotics or anorectics. Multiplying these figures by the population of the rest of Europe and North America yields a truly mind-boggling figure. Many of these drugs are taken long-term. Williams (1987) and Mellinger *et al* (1984) report that 20%–25% of patients prescribed antidepressants or minor tranquillisers continue them for a year or more – often for many years (Fig. 3). In the case of benzodiazepines, continued use is mainly due to drug dependence (Owen & Tyrer, 1983). However, it is not uncommon to see people (usually women) who have been taking antidepressants continuously for many years, with or without benzodiazepines (and some of these get withdrawal symptoms when they stop).

With regard to epidemiology, the most studied of the psychotropic drugs are the tranquillisers, and many investigations have confirmed the greater use of these drugs by women than by men. In a cross-national survey of anxiolytic/sedative use in 1980–81, Balter *et al* (1984) (Table 1), found that the highest use was in Belgium (12.9% of men and 21.4% of women) and the lowest was in Holland (5.7% of men and 9.1% of women). In the USA, 8.5% of men and 16.9% of women were users, while in the UK 6.7% of men and 15.3% of women had used this type of medication in the previous year. In all countries, the female : male ratio was close to 2 : 1. Prescription rates for anxiolytics and sedatives increase with age of patients, and Taylor (1987) estimated that the 13 million British women over 40 years old receive almost 60% of all benzodiazepines prescribed for the UK population, while the five million women aged over 65 years consume about 40% of all prescribed benzodiazepine hypnotics.

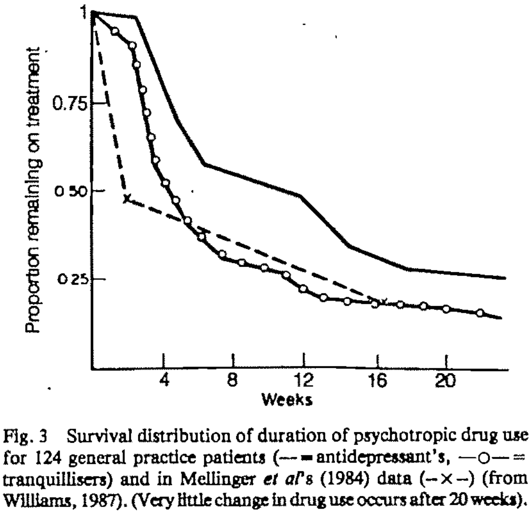

Fig. 3 Survival distribution of duration of psychotropic drug use for 124 general practice patients (— = antidepressant's, —○— = tranquillisers) and in Mellinger *et al*'s (1984) data (– × –) (from Williams, 1987). (Very little change in drug use occurs after 20 weeks).

Tranquilliser use is associated with complaints of ill health. Ashton & Golding (1989) noted that anxiolytic/hypnotic users in the UK (two thirds of whom were women) had highly significantly more symptoms of psychological and physical malaise than non-users. Several studies show that women are more likely than men to complain of symptoms, especially psychological ones. For example, Uhlenhuth *et al* (1983) investigated a cross-sectional sample of a nationwide survey of psychotropic drug use in the US in 1979. They developed a method of classifying symptoms in the general population into syndromes which corresponded with DSM–III criteria (American Psychiatric Association, 1980) for diagnoses of psychiatric illness. As a result of extensive home interviews (using the Hopkins Symptoms Checklist and other tests) with 3161 non-institutionalised adults aged 18–79 years, they identified four syndromes corresponding with DSM–III counterparts (major depression, agoraphobia/panic, other phobias, generalised anxiety) and a miscellaneous category of other high psychiatric distress (Table 2). They found that the prevalence of psychiatric syndromes in all categories was higher in women. The female : male ratio was 2.5 for major depression, 3.6 for agoraphobia/panic, 2.4 for other phobias, 1.9 for generalised anxiety and 1.5 for other

Table 2
Prevalence of psychiatric syndromes in previous year (1979) in 3161 non-institutionalised US adults aged 18–76 years (data from Uhlenhuth *et al*, 1983).

Syndrome (DSM-III counterpart)	Men (n=1431) %	Women (n=1730) %	All (n=3161) %	Female : male ratio
Major depression	2.8	6.9	5.1	2.5
Agoraphobia/panic	0.5	1.8	1.2	3.6
Other phobia	1.3	3.1	2.3	2.4
Generalised anxiety	4.3	8.0	6.4	1.9
Other high psychiatric distress	8.4	12.6	10.7	1.5
No major symptoms	82.8	67.5	74.4	0.8

high psychiatric distress. It is noteworthy that over 25% of this general population was suffering from some form of psychiatric distress, and the prevalence was over twice as high in women.

Table 3 shows the use of psychotropic drugs in Uhlenhuth *et al's* (1983) sample. It would appear that drug use was not always appropriate or effective. For example, only 11% of the individuals with major depression were using antidepressant drugs, although 29% were using anxiolytics/hypnotics; and 69% of them took no psychotropic drugs at all. The 36% of those with generalised anxiety who used anxiolytics or sedatives still had anxiety. Of the agoraphobics, 58% used anxiolytics and 11% antipsychotics, which did not appear to be effective; only 8% used antidepressants. There is unfortunately no record of non-drug treatments, and the sex ratio of drug treatment is not specifically recorded. However, the authors reasonably concluded that the majority of people with major psychiatric disorders were not receiving the most appropriate treatment and that many of these disorders go unrecognised.

In a study of London general practices Shepherd *et al*, (1966) found that 7% of men and 13% of women 'usually felt unhappy', 2% and 6% respectively 'felt so unhappy they wished they were dead', 1.8% and 2.5% 'always felt miserable and blue', and 2.7% and 4.4% 'felt that life was entirely hopeless'. Men take more definitive action, however: according to the average figures (Her Majesty's Stationery Office, 1974–78) of the Registrar General, the suicide rate was 9.7 per 100 000 for men compared with 6.2 for women, although more women presented with self-harm/self-poisoning. In addition to unhappiness, 10% of men over 65 and 30% of women reported difficulty in getting to sleep (McGhie & Russell, 1962).

Young women, too, appear to voice more psychological complaints than young men. Table 4 shows drug-taking habits in medical and non-medical students at Newcastle University in 1983–84 (Golding & Cornish, 1987). Asked if they had ever been prescribed minor tranquillisers, 14.6% and 10.3% of the medical and non-medical female students said yes, compared with 4.2% and 6.5% of the men, respectively. Thus, even at the average age of 19 years, women are more likely to go to their general practitioners and be prescribed a tranquilliser than men. Alcohol consumption had the opposite gender distribution, being greater in men (this is true of all ages: Taylor, 1987); the percentage of smokers was about the same in both sexes. It was reassuring to find that smoking, drinking, cannabis use and the use of other illicit drugs was much lower among medical students than non-medical students of both sexes.

All the studies quoted above (and many more) show clearly that women, at all ages, consume twice as many psychotropic drugs as men; that psychiatric illness (depression and anxiety) are apparently about

Table 3
Percentage of those with psychiatric syndromes in Uhlenhuth *et al's* (1983) sample who used psychotropic drugs

Drug type	Syndromes Major depression %	Agoraphobia/ panic %	Other phobia %	Generalised anxiety %	Other high distress %
Anxiolytic/Hypnotic	29	58	21	36	23
Antidepressant	11	8	1	3	3
Antipsychotic	3	11	1	3	2
No psychotropic	69	41	79	62	74

Table 4
Drug taking in male (M) and female (F) medical and non-medical students at Newcastle University (data from Golding & Cornish, 1987)

	Medical students		Other students	
	M (*n* = 119)	F (*n* = 96)	M (*n* = 77)	F (*n* = 68)
% taking tranquillisers (prescribed)	4.2	14.6	6.6	10.3
Alcohol: units/day	0.9	0.4	1.6	0.9
% smokers	10.9	11.5	27.3	29.4
% taking cannabis (ever)	26.1	14.6	49.4	44.1
% taking other illicit drugs (ever)	4.2	2.1	28.6	19.1

twice as common in women, and that women are more likely than men to voice psychological complaints to their doctors. Is their increased psychotropic drug consumption simply the inevitable and rational result of a greater prevalence of psychiatric or psychological illness?

Probably the situation is not that simple. To take the example of a physical disease, the Boston study (Greenblatt *et al*, 1975) showed that even among hospital admissions for somatic diseases (gastrointestinal, cardiovascular, etc.) women were twice as likely as men to be taking psychotropic drugs. There are, of course, some physical conditions which only occur in women: Parish's study in London (Parish, 1971) showed that one in 20 of all prescribed psychotropic drugs were for disorders of menstruation (including dysmenorrhoea and premenstrual tension), or pregnancy (hyperemesis gravidarum or post puerperal depression), or related to the menopause. Another 7% of psychotropic drug prescriptions were for obesity, and here females outnumbered males by a ratio of 7 : 1. It could be argued that women are more prone to develop psychiatric complications along with physical diseases, but there does not seem to be a corresponding proportion of psychotropic prescribing for purely masculine complaints such as prostatic enlargement or impotence.

Many people have suggested that one important factor might be doctors' attitudes to patients. On this sort of topic, hard evidence is difficult to obtain: information is anecdotal and speculative. Doctors' attitudes are illustrated in a recent article by a female consultant haematologist (Brozovic, 1989). She records that as a young research assistant in a London hospital she developed abdominal and back pain. After tolerating it for a few days, she consulted a senior colleague, a gastroenterologist. He was kind, examined her and talked to her for half an hour. He said that she had irritable bowel syndrome and discussed the stresses that young married women in medicine had to contend with. The next morning she had high fever, haematuria and a clear case of pyelonephritis.

A few years later, this same female doctor awoke with chest pain and shortness of breath. She crawled to the Casualty Department where they said she was hyperventilating and she was told to breathe into a paper bag. A few days later it became clear that she had glandular fever and pneumonia. There are many similar reports from women diagnosed by male doctors to have psychological complaints which have later turned out to be somatic illness. Many of these women have been prescribed psychotropic drugs.

But it is not only male doctors: the same female doctor mentioned above realised she was no different from her male colleagues. She reports that for many years she had been following a female patient with benign paraproteinaemia. One day, after a routine blood test, this patient complained of nausea, thirst, dry mouth, aches and pains all over, insomnia and tremor. It also turned out that she had recently lost her father. The doctor talked to her for a long time about the effects of bereavement and arranged to see her again in a year. After she had left, the laboratory telephoned to say that the patient had gross hypercalcaemia and hyperproteinaemia, and had developed a very malignant form of multiple myeloma.

Brozovic (1989) speculates that doctors in general may have a need to assert a paternalistic role which characterises women as weak, vulnerable and emotional. Alternatively, perhaps the doctors themselves need reassurance that women are basically strong and indestructible: all women need to do is to pull themselves together, to continue acting as carers, handmaidens and general support crew!

In any case it does appear to be true that doctors are more likely to perceive illness in women as having a psychological rather than a physical basis, and this perception makes them more likely to prescribe psychotropic drugs. In this they may be influenced by medical advertising. Prather & Fidell (1975), in a study of medical advertisements, found that advertisements for psychoactive drugs showed significantly more women, while advertisements for non-psychoactive drugs showed significantly more men. Examples included: an advertisement for an anorectic in which a very attractive woman in a seductive pose says "Dear doctor, you made me what I am today – a whole lot slimmer"; an advertisement for a tranquilliser which shows a bride in obvious distress, at the altar with the groom, and which includes the caption: "When diarrhoea wrings the wedding belle . . ."; and a further tranquilliser advertisement which includes a picture of a family with the focus on the woman and the caption: "Treat one . . . six people benefit". Whether such advertisements are leading the doctors, or whether they are simply following medical practice is debatable.

Another factor influencing prescriptions of drugs may be women's attitudes. These have been examined by Cooperstock (1979) and Cooperstock & Lennard (1979) who argued that women use more psychotropic drugs than men because society permits them: (a) to express feelings such as anxiety; (b) to perceive emotional problems in themselves; and (c) to use medical care for emotional problems. To this may be added the argument that society permits men (who are less introspective and less confined to the home) other outlets – especially the use of alcohol. It is suggested that men tend to go out and use alcohol for coping with stress while women tend to stay at home and use tranquillisers – and it is true that the pattern for alcohol use by age and sex is a mirror image of the pattern for tranquilliser use (Taylor, 1987).

Cooperstock & Lennard (1979) conducted group interviews with tranquilliser users in Canada. They found that the women tended to use tranquillisers because they were in an inescapable situation in trying to keep the family together. One woman said:

> "I take valium to protect the family from my irritability because the kids are kids . . . I suppose I overreact but because I overreact is no reason for my family to suffer . . . so I take the valium to keep me calm. The kids get on [my husband's] nerves too. But he will not take anything – he blows his top. When I blow my top I am told to settle down. When he does it is perfectly alright. He's the slow volcano kind, but when he loses it, oh boy! He can blow but I can't . . . One of these days I am going to leave the whole kit and kaboodle and walk out. Then maybe I won't need any more valium" (Cooperstock & Lennard, 1979, p. 332).

The men in Cooperstock & Lennard's study, on the other hand, tended to take tranquillisers to cope with work, but could usually find an escape from the home.

These sociological studies are interesting: they do not necessarily prove anything but they perhaps shed some light on prescribing habits.

Conclusions

Taking all the evidence together, it is possible to suggest the following lines for discussion and further research.

(a) Psychotropic drugs are not always appropriately prescribed. Regardless of their own or the patient's sex, doctors should use such drugs where there are clear indications such as depression, but should seek better solutions than drugs for social problems. Tranquillisers have long been grossly overprescribed and it is clear that not only do they not solve social problems, but may often add to them by causing drug dependence.

(b) It seems likely that psychiatric or psychological illness is overdiagnosed in women, and overtreated with psychotropic drugs. Possibly these illnesses are underdiagnosed in men. The generally accepted 2 : 1 female : male ratio for the incidence of depression and anxiety may not be correct, since the men are less likely to seek medical attention.

(c) There may well also be genetic and hormonal differences affecting behaviour. There are known to be sex differences in the brain before birth and there are sex differences in cognitive function in young children – females being better at linguistic and males at visuospatial tasks. There is little information on emotional differences between the sexes, and the female limbic system has never been explored.

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Alcohol and Drug Misuse Among Women – An Overview

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Most research into substance misuse has focused on men but the problem among women is considerable and the social consequences and causation differ between the sexes. In the US, one-third of alcohol abusers are women and in the UK 1% of women are estimated to be drinking at a dangerous level. Drug and alcohol misuse holds additional problems for women since abusers tend to be of childbearing age. Rehabilitation units and prevention strategies would benefit more women substance abusers if they were tailored to suit their specific needs.

The misuse of any psychoactive substance by women tends to produce tangled and contradictory reactions from society. Pity and concern are, not infrequently, mingled with derision and contempt. Inebriety, femininity, motherhood and work performance do not in general go well together. The portrayal of the stereotypical woman alcoholic includes numerous emotive references such as "the hand that rocks the cradle shaky from drink" (Curlee, 1967) or descriptions of the "fallen angel". The idealised woman is despised for behaving in an unseemly manner. The drug addict is sometimes depicted as both depraved and irresponsible. Women under the influence of drugs or alcohol are seen as unable to fulfil their mothering and domestic role and the disinhibiting effects of drugs may generate excessive and degrading promiscuity and other unacceptable, sometimes criminal, behaviour.

It will not be argued here that alcohol and drug misuse does not lead to serious impairment in a person's functioning, but that it is essential to distinguish between the facts and fictions of women's addiction. Attention must be focused on removing the stigma and marginalisation that has been attached to substance-abusing women, and a serious attempt must be made to provide them with help and understanding and, if possible, prevent the development of addiction problems.

In Britain, as in other countries, there has been a considerable increase in awareness of women's concerns in the last 20 years. Attention has been paid to women's position in the home and in the workplace, and to their economic, biological and social role. Nevertheless, there has been only a limited interest in women who misuse alcohol and other drugs. To date most research, policy and treatment initiatives in respect of substance misuse has focused on men and thus the special features of women substance misusers have received scant attention. However, the extent of problem drug and alcohol use among women is considerable and is believed to be on the increase.

Different drugs, different problems?

Women who misuse mood-altering substances, be they alcohol or other drugs, face many difficulties, some of which are specific to the drug of abuse, and many that are not. Different chemical substances affect the body differently and produce varied physical consequences. Different life-styles may be associated with the drug of abuse. For example, the purchase and possession of heroin, cocaine and 'crack' are illegal and the cost of these drugs is high. Thus, obtaining and paying for supplies may force the user into the margins of society and into a delinquent life-style. The use of illicit drugs is often furtive and executed in unhygienic conditions, thereby leading to emotional and health complications.

Although a woman may purchase her daily supplies of alcohol with the family shopping, the consequences of excessive drinking on her life-style, health and general capacity to cope, as well as on those around her, may be just as devastating.

Defining alcohol and drug misuse

Although the misuse of alcohol and the misuse of other drugs have much in common, it is usual to discuss them separately, not only because some of the issues presented by their misuse are different, but also because they are subject to different systems of regulation. In this paper it is proposed to offer an overview of both alcohol and drug problems as these affect women, focusing on social and psychological aspects while biological aspects are given less prominence.

Psychoactive drugs

Many potentially addictive drugs are used both in medical treatment and for non-medical or recreational purposes. Moreover, some drugs which are regarded as problematic in the West may not be so in other societies (e.g. cocaine is regarded as acceptable when used by the inhabitants of the high Andes in South America in the form of coca chewing). What is considered as misuse is determined, therefore, not only by the chemistry of the drug but also by the social context, frequency and quantity of its use. It is therefore important to clarify what is referred to here as drug misuse.

In Britain, the Royal College of Psychiatrists (1987) offered a useful definition of drug misuse, thereby identifying what the target of social and medical intervention ought to be:

> "Drug Misuse is any taking of a drug which harms or threatens to harm the physical or mental health or social well being of an individual, or other individuals, or of society at large, or which is illegal."

Much of the data presented here is derived from research on women who use opioids and cocaine. This paper does not discuss problems that arise specifically from the misuse of prescribed psychoactive drugs.

Alcohol

Alcohol is a complex subject to study because it can be used both moderately, in a socially acceptable way, and in an excessive and destructive way. In most Western societies the social use of alcohol by adults is commonplace and acceptable. However, the demarcation between what is regarded as social drinking and the use of alcohol that goes beyond this produces problems of definition.

Guidelines for acceptable drinking

In order to understand 'problem drinking' it is useful to describe what is generally accepted in Britain as safe, 'normal' or acceptable drinking.

One must note that what may be a safe drinking level for one person may lead another into difficulties. Men and women differ markedly in the quantities of alcohol which they can safely consume. The Royal College of Physicians (1987) suggested general guidelines for safe levels of alcohol consumption: 14 units of alcohol for women and 21 for men, per week. (A unit is 8 g pure alcohol, approximately equivalent to one glass of wine, half a pint of ordinary beer, one measure (1/6 gill) of spirits or one glass of sherry.) The report also suggests that drinking 14–35 units per week is hazardous for women, and 35 or more units is definitely dangerous.

During pregnancy the safe limits are much lower, because of the threat to the foetus. The Royal College of Physicians suggests that for pregnant women 10 units weekly is the safe limit. It quotes the findings of a study of 1000 Scottish women which demonstrated that when the maximum drinking during pregnancy was less than 10 units of alcohol per week it did not cause foetal harm. Nevertheless, many physicians would argue that no alcohol at all is preferable during pregnancy.

Problem drinking and dependent drinking

The Royal College of General Practitioners (1986) has sought to define 'problem drinking' and 'dependent drinking'.

A problem drinker was characterised as "someone who experiences physical, psychological, social, family, occupational, financial or legal problems attributable to drinking". There are wide variations, some cultural and some individually determined, in alcohol consumption and in the interpretation of what constitutes 'problem drinking'. However, it is generally accepted that 'problem drinking' encompasses the more lasting consequences of heavy drinking (more than an occasional hangover or the very occasional getting drunk).

A dependent drinker is "someone who has a compulsion to drink, takes roughly the same amount each day, has increased tolerance to alcohol in the early stages and reduced tolerance later: suffers withdrawal symptoms when alcohol is stopped which is relieved by consuming more; in whom drinking takes precedence over other activity and who tends to resume drinking after a period of abstinence".

These different clinical profiles of people presenting with what are globally referred to as drinking problems indicate that a variety of treatment responses are needed. Edwards (1988) suggested that "what is needed for treating the commoner and milder manifestations of excessive drinking is demystification, destigmatisation, and common sense. . . . As to what treatment works for a high degree of dependence, here the debate is particularly open. Intensity of dependence is not the only relevant criterion that bears on choice of treatment, but the view that abstinence is the best choice for the highly dependent drinker has again received wide support."

An overview of the facts of women's substance misuse – how big is the problem?

Alcohol

The extent of alcohol problems among women is difficult to ascertain. Predictably, there is a large grey area between socially acceptable drinking and serious 'problem drinking' or 'dependent drinking'. Recent studies undertaken by the Office of Population Censuses and Surveys (OPCS) (Goddard & Ikin, 1988) estimate that 1% (250 000) of women in Britain are drinking at a theoretically dangerous level of more than 35 units per week, and a further 2 million women (8%) are drinking above 14 units per week (National Association of Health Authorities, 1989). This confirms an earlier study of drinking in one week in England and Wales also undertaken by the OPCS (Wilson, 1980) which found that 10% of women drank 11–20 units per week and 2% drank 21–35 units.

Figures from the USA demonstrate the magnitude of the problem and are taken from a national household survey (National Institute on Alcohol Abuse and Alcoholism, 1985). These show that as many as six million American women are drinking excessively (2.5 million have alcohol problems and a further 3.3 million are probably alcohol dependent). Altogether about one-third of all those who have a drink problem in the USA are women.

Research both in the USA (Wilsnack *et al*, 1984; Wilsnack *et al*, 1984/85) and in Britain (Breeze, 1985) shows that although women's overall drinking consumption is not on the increase, there have been important changes in the patterns and age distribution of women's alcohol intake. Wilsnack, in a study of 917 American women found that, overall, women drank less than men. Of her sample, 39% were abstainers and a further 38% were light drinkers. Drinking increased among middle-aged women, 35–64 years, and heavy drinking increased in the 35–49 age group. Those at highest risk of alcohol problems were younger women and those who remained unmarried, were divorced or separated, or were unemployed. Consumption patterns among adolescent girls in the USA increasingly resemble those of adolescent boys, with fewer young women total abstainers, thus portending an increase of alcohol problems in the future (Johnston *et al*, 1985).

In the UK, alcohol consumption among younger women is rising significantly with the heaviest drinkers aged under 25, employed and unmarried (Breeze, 1985). Furthermore, research undertaken by OPCS (Goddard & Ikin, 1988) indicates that women's average weekly consumption is now 4.8 units per week. While men aged 18–24 have cut their drinking from 26 units to 21 units weekly in the last ten years, average consumption in young women has risen from 4.5 units to 6 units weekly. This is a disturbing trend because as more women are entering the workforce we can expect an overall increase in drinking problems among women in future.

Drugs

There is even less precise information about the extent of drug use than about alcohol. Since the drugs which are discussed here are used illicitly and not in the course of medical treatment, many drug users do not come to public attention, or if they do, only after a long period of drug taking (Sheehan *et al*, 1988).

The number of women experiencing problems from drug taking has been estimated using many diverse indicators. Most of these data pertain to opioid users. It has been consistently observed in Britain (Glanz & Taylor, 1986; Sheehan *et al*, 1988) that there is a ratio of approximately one woman to every three men coming to treatment for drug problems. It is suggested that if this reflects the numbers of people actually misusing drugs then probably a quarter of the total population of drug takers in Britain are women. It has been estimated that 100 000 people in Britain use heroin on a heavy and regular basis during a year and that recreational use of heroin has also developed among people in their late teens who sniff or smoke the drug but sometimes inject (Institute for the Study of Drug Dependence, 1990).

Thus, somewhere between 25 000 and 33 000 women in Britain have an opiate drug problem, and there are many more who are misusing other non-prescribed drugs. It is impossible to say whether the prevalence of drug misuse in women is growing or whether it has peaked, though the most recent figures of drug addicts notified to the Home Office by doctors (Home Office, 1990) showed a slight increase compared with previous years. (Out of a total of 14 785 notified addicts, 4306 were women, of whom about half were injectors.)

Consequences of alcohol and drug misuse

There are numerous social and physical consequences from the excessive use of psychoactive substances. Many are common to both men and women although some are gender specific. Some have a direct effect on the woman herself and some have an indirect, although potent, effect on her family and social network. The social consequences are similar whichever drug is being abused, but the physical consequences vary in accordance to the specific drug.

Physical consequences of alcohol misuse

Alcoholism in women is associated with high rates of gynaecological, reproductive and sexual difficulties. In the USA, the 1981 National Survey (Wilsnack *et al*, 1984) showed that there was a positive correlation between women's drinking levels and their reports of dysmenorrhoea, heavy menstrual flow, pre-menstrual discomfort and sexual dysfunction – including low rates of sexual satisfaction. However, at present the mechanisms of these associations are unclear, and it is believed that both biological and psychological causes are probably involved (Roman, 1988).

In the same review of alcoholism in women, Roman asserted that women alcoholics tend to have a more personally destructive drinking career than men. Indeed there is substantial evidence that women experience alcohol-related problems earlier in their drinking career and most probably as a result of less drinking than men. This is a phenomenon that is generally referred to as the "telescoping of problems" (Piazza *et al*, 1989). The explanations for this are many and complex, and not altogether clear. In part they lie in women's lower body weight, less body water and higher percentage of fatty tissue (Kalant, 1971). This distinction may also lie, however, in the social structures and social conditions in which women find themselves.

Mortality from alcohol

For women who develop alcohol dependence, life expectancy is markedly curtailed. Although based on a relatively small number of studies of women alcholics who had been in hospital for treatment of alcoholism, it has been suggested from a seven-year follow-up of 107 alcoholic women in the USA (Smith *et al*, 1983) that nearly a third had died – 4.5 times the expected rate. Another study showed that at 12-year follow-up of women in-patients, one-third had died (Smith & Cloninger, 1981). The average life span of these women was decreased by 15 years.

In England and Wales in 1988, 226 women died from 'alcohol-related causes' (e.g. alcohol dependence syndrome, non-dependent abuse of alcohol, accidental poisoning by alcohol, alcoholic cardiomyopathy) (Office of Population Censuses and Surveys, 1990). The figure for the same year for men was 429. In addition, the number of deaths from alcoholic cirrhosis of the liver and alcoholic liver damage was 400 (compared with 651 men) suggesting that women are catching up with men in experiencing severe consequences of alcohol. The overall death rate for women dying of alcohol-related problems was calculated as 2 per 100 000 population compared with 4.3 per 100 000 for men (National Association of Health Authorities, 1989). However, these figures disguise the fact that, in addition, more die as an indirect consequence of alcohol misuse (e.g. accidents, suicides, circulatory disorders).

Damage to the unborn child from alcohol

It has been established (Abel, 1984; Kruse, 1984) that there is a link between heavy and persistent drinking during pregnancy and damage to the foetus. Moderate drinking is, however, thought to be unlikely to cause foetal harm.

The foetal alcohol syndrome (FAS), which consists of serious damage to the child, is a relatively rare condition and varies across cultures and ethnic groups. Researchers in the USA estimate that FAS occurs in 1–3 out of every 1000 live births worldwide, but among problem drinkers the rate has been shown to be as high as 23–29 per 1000 births (US Department of Health & Human Services, 1983). Information from European countries suggests that northern France has an estimated rate of 1/1000 incidence of FAS and Sweden a rate of 1/600. In the UK the rates appear to vary and seem to be concentrated in areas of heavy drinking and poor nutrition – the West of Scotland, Liverpool and Belfast – although it is rare in London (Barrison *et al*, 1985).

The severity of the syndrome is subject to wide variations. The major features of FAS include low birth weight, growth retardation, mental handicap and other neurological disorders, and heart defects. Most common is low birth weight which, although not fatal in itself, may lead to complications rendering the new-born infant more vulnerable to childhood disorders, and may impede normal development.

'Foetal alcohol effects' – less severe alcohol-related birth defects that occur in mothers who drink smaller amounts – are said to be more common than FAS (National Institute on Alcohol Abuse and Alcoholism, 1985).

Physical consequences of drug misuse

Women who misuse drugs are subject to the same risks of ill health and overdose deaths as their male counterparts, as well as the dangers of severe weight loss, hepatitis B, muscle wasting, and other diseases related to a chaotic life-style, poor and erratic nutrition and lack of financial resources. When women turn to prostitution in order to finance their addiction, they put themselves at the additional risk of contracting sexually transmitted diseases. Since the advent of HIV these women are at risk not only from casual sex, but also, in common with all drug users, male or female, from the casual sharing of syringes with others.

Pregnancy and drug misuse

Women who misuse opioids are often of childbearing age. There is concern about the effects of drugs on future offspring. While congenital abnormalities occur primarily during early pregnancy, some drugs can affect the growth of the foetus and its post-natal behavioural and mental performance when exposure occurs at later stages of pregnancy. Even after delivery, maternally ingested drugs can gain entrance to the neonate through the mother's milk (National Institute on Drug Abuse, 1979).

A worrying number of pregnant addicts do not attend pre-natal clinics partly because of their chaotic life-styles and partly because they fear the reaction of the authorities once their addiction is known (Social Services Committee, 1985).

Opioid misusers often give birth to small-for-date, sometimes premature babies, who have to be treated for drug withdrawal symptoms (Gerada *et al*, 1990). The same applies to women who are treated with the synthetic opiate – methadone – during pregnancy (Rosen & Johnson, 1985).

Overall, it is believed that "developmental outcome is the result of an interaction of a variety of factors. In utero exposure to certain substances . . . represents a significant source of biological vulnerability . . . [but] the valid identification of specific drugs associated with a behavioural or structural teratogenic effect on the fetus remains a source of methodological concern . . . many conditions associated with poor developmental outcome are more prevalent among people living in poverty, which further confounds the effects of pre-natal drug exposure" (Zuckerman, 1985).

The risks of HIV infection

The risk of an infected pregnant drug taker transmitting the HIV virus to her child is considerable. Very few such cases had been reported in Britain before 1988. The Advisory Council on the Misuse of Drugs (ACMD, 1988) report gave a figure of 80 babies known to have been born with the HIV virus although not all the mothers were drug users. It has been noted that not all infected mothers transmit the virus. ACMD believed that the likelihood of transmission from infected mothers to their babies is between 25% and 40%.

Social consequences of alcohol and drug misuse

These can be dramatic and devastating. The "career of narrowing options" is the way in which Rosenbaum (1981) characterised the world of a heroin addict. Initially, taking drugs might give a woman the feeling that her horizons are expanding. She may feel that she is learning about a new world, experiencing new sensations and joining an exciting alternative life-style. However, as she becomes drug or alcohol dependent the sheer need for the daily drug or alcohol – to stave off withdrawal and to make her feel normal – becomes an increasingly hopeless and unsatisfactory life experience.

For many female heroin or cocaine addicts the financial problem of finding the money for daily drugs usually means that regular employment is not practical, and that they need to resort to criminal activities, or to prostitution, in order to finance their habit, or be totally dependent on their male partners for both money and drugs.

The consequences of alcohol and drug misuse on relationships

Living in a close intimate relationship is difficult if drugs or alcohol are being abused. Many women who have such a problem live with men who are similarly misusing various substances. Not surprisingly the rates for divorce or separation are higher in this group than in the population as a whole. One review of the research on alcoholism and marriage (Paolino *et al*, 1978) revealed that women alcoholics are four times more likely to divorce than non-alcoholics, although overall there are no very conclusive data on the causal relationship between alcoholism or drug misuse and marriage breakdown.

Children

Much has been written about the effect of a woman's drinking or drug taking on her children (Williams & Klerman, 1985; Deren, 1986). Effects range from actual physical neglect by mothers not competent to be carers to more subtle, but nevertheless potent, emotional neglect. It has been shown that these children do not perform well at school and show emotional and learning difficulties when growing up. Parental substance misuse is one of the most commonly described risk factors for children themselves abusing drugs in later life. It has been estimated, for example, that somewhere between 20% and 30% of daughters of women alcoholics become alcoholics themselves (Youcha, 1986). The risks for children of an unsatisfactory emotional environment culminating in family breakdown are very real.

The antecedents of alcohol and drug use

It has been possible to learn from women who have experienced drug or alcohol problems about their childhood and family experiences and to examine their explanations about their behaviour. Much effort has gone into trying to determine whether those who misuse drugs have discernible personality characteristics or significant common factors in their histories. However, the problems with a retrospective reconstruction of life events are many, and it is not possible to attribute causal links. Most difficult is the fact that there are some who have experienced similar difficulties, or who have a similar personality profile, who did not develop a substance abuse problem.

With these provisos it is nevertheless useful to look at some of the antecedent factors in the histories of those who develop alcohol and drug problems, if only to see whether any prevention strategies might be applied, and to identify treatment needs.

Since it is impossible to identify one factor that inevitably leads someone into a career of drug or alcohol misuse some researchers (Bry, 1983) have suggested a multiple risk-factor hypothesis. She proposed that there is no single factor which is sufficiently important on its own, but a number of different factors which could be present in different combinations.

Some recurring themes have been found in the histories of women with drug and alcohol problems. During their childhood many experienced parental alcohol and/or drug misuse (Rachal *et al*, 1982) and a lack of cohesion in the family of origin where parents were in conflict about control issues and questions of child rearing. Binion (1979) concluded that women addicts came from more disturbed families, and more frequently from broken homes, and thus probably experienced high levels of separation from one or other parent. Binion (1982) suggested further that among a sample of heroin addicts there were sex differences in the perceptions of family interaction. Women were more likely than men to report negative impressions of their childhood and to have noticed differences in adult's treatment and expectations of boys and girls. She concluded that initial drug use for women was closely related to interpersonal affiliation issues and that women were more likely than men to seek out an addict peer group as a reaction to unhappy family situations.

There is increasing evidence that addicted women have a higher than expected rate of early sexual abuse (Rohsenow *et al*, 1988). Although the literature on this matter is still small, the results strongly suggest that for a subgroup of drug misusers, sexual abuse is a strong contributory factor in the aetiology and maintenance of drug misuse.

It is thus noticeable that women who become substance misusers frequently come from unstable and conflicted families where standards of care were poor and where the demands made upon the growing girl were erratic and at times inappropriate.

Treatment and rehabilitation

Given the complexity of the factors leading to drug and alcohol misuse, the variety of consequences of such behaviour, and the diversity of psychological and social difficulties manifested by users, it is obvious that women have numerous treatment needs. Insufficient attention has been given to women's special needs in treatment. "The needle world is a man's world" is how Nadeau (1978) characterised drug treatment. Perhaps the alcohol treatment world is similarly biased to the 'male drinking culture'. Thus, most treatment facilities have been designed with men and their needs in mind.

What is available?

In Britain, as in many other countries, there exists a range of facilities for drug and alcohol misusers. In general these are patchy and not uniformly available, and are traditionally sited in large urban conurbations and areas that are clearly identifiable as having the greatest need. There are few facilities that are for women only. Indeed not all women would necessarily choose such a service. However, from the research literature it is clear that women have special needs in treatment which are seldom met (Reed, 1981). In some residential projects the scant numbers of women clients has encouraged the staff to question women's obvious reluctance to come forward for help and to look for ways of attracting and keeping women clients.

Medical services

The general practitioner is usually in the forefront of the medical response to alcohol and drug problems and works alongside the specialist medical services in hospitals as part of the National Health Service provision. Hospital services include out-patient and in-patient programmes of detoxification from drugs and alcohol plus counselling and overall health care. Most of the clinical services are staffed by multi-disciplinary teams that include doctors, social workers, nurses, etc. There are no clinics that specialise in helping women with drug or alcohol problems. Some of the clinical services provide the base for alcohol community teams or community drug teams who work both within the hospital walls and in the community.

Although the overall aim is to help drug-dependent or alcohol-dependent men and women to stop misusing substances, opiate misusers are at times offered help in the form of long-term treatment with a synthetic opiate substitute – methadone. This is prescribed in non-injectable, linctus form and is taken daily – thus avoiding the need for frequent injecting.

In general, National Health Service provision for alcohol and drug misusers (usually offered in separate clinical facilities) is provided in outpatient departments. Alcohol and drug misusers are invariably encouraged to attend either Alcoholics Anonymous (AA) or Narcotics Anonymous (NA) meetings.

Residential hostel facilities

Residential facilities are offered in the voluntary or private sector. There are a number of therapeutic communities that offer help mostly to drug users. These establishments offer a relatively long and intensive rehabilitation programme, ranging from 9 to 12 months based on the self-help principle. Its underlying philosophy is to view drug misuse as 'deviant behaviour' reflecting impeded personality development and deficits in social and educational skills (De Leon, 1984). There is another model of residential treatment known as the Minnesota treatment. It offers a shorter programme of about four to six weeks using predominantly AA and NA ideas (Cook, 1988). They offer help to people who suffer from either alcohol or drug problems.

Other help

Other sources of help for those who experience problems from substance abuse include 'shopfronts', or outreach street agencies, who try to encourage those with difficulties to come to them and begin the help-seeking process. There are a few day programmes located in the community, providing shelter and a non-threatening environment in which to begin the process of treatment and rehabilitation. Finally, there are the self-help groups mentioned – AA, NA and others.

Getting into treatment

The first challenge is to try to attract women to use treatment. There is some evidence that many women fail to make use of services. Both men and women tend to misuse drugs for very long periods before making their first treatment approach to a helping agency. It is also known that women consult their general practitioners for a multitude of reasons which disguise a drink or drug problem.

Thom (1986), in her study at a London alcohol clinic, identified some of the major difficulties in help seeking reported by women. Most interesting is her conclusion that many women who drink excessively and who suffer from the consequences of that behaviour do not identify themselves as requiring alcohol-focused treatment since they see their difficulties as emanating from their social or psychological problems. They are consequently reluctant to make use of specialist services. The implications are clear: women could be prevailed upon to use generic services, provided the generalist were trained and willing to help.

The barriers identified by many drug-taking women focus most on concerns about the effects of disclosure of their problems to the authorities. Fears of interference by the social services, or the medical services, are considerable, as are concerns about having their children put into care against their wishes. The fear of authority is so considerable that some women choose to go through an entire pregnancy without medical care (Social Services Committee, 1985).

Some specific treatment needs

Based on what we know about the profiles of women who misuse drugs and alcohol, and on the information that many women fail to come to treatment or to engage in treatment after an initial approach, it is possible to identify some areas that need attention.

Reviewing studies from the USA, Burt *et al* (1985) concluded that many programmes were better geared to younger women, aged under 25, and that older women are, for reasons that are not clear, not coming forward for treatment. They concluded that long-term, opiate-orientated treatment programmes that exist may not be appropriate for a large segment of the drug-misusing female population.

Depression and anxiety, other mental health problems such as low self-esteem, feelings of worthlessness, guilt and anxiety about their children, feelings of sexual inadequacy etc. often accompany drug and alcohol abuse. Burt *et al* (1985) make it clear that women must be helped to tackle these problems if they are to solve their drug or alcohol problems. The simple prescribing of drugs to help withdrawal or a period in an institution that is dominated by men and which operates a hierarchical and competitive treatment ideology is unlikely to be helpful. Specific advice about drinking or drug taking may not suffice since these are not seen by many women as their predominant problems.

To cope with these gender-specific needs one can suggest a number of approaches, such as women's groups, women therapists, women-only facilities, counselling that takes a feminine perspective into consideration, facilities with flexible opening times to take child-care difficulties into account, facilities where women will feel safe, protected and understood. Practical help in education, housing and employment is also important, since many drug-dependent women have a long history of dependence on men (Reed, 1981).

The way ahead

Marsha Rosenbaum's book *Women on Heroin* summed up the career of a heroin-addicted woman; and for heroin one can substitute alcohol, since the experiences described below will be easily recognised by most women alcoholics.

> "... heroin expands her life options in the initial stages and that is the essence of its social attraction. Yet with progressively further immersion in the heroin world, the social, psychological exigencies of heroin create an option 'funnel' for the woman addict. Through this funnel the addict's life options are gradually reduced until she is functionally incarcerated in an invisible prison. Ultimately, the woman addict is locked into the heroin world and locked out of the conventional world."

This exclusion from the conventional world, this marginalisation of women, fearful about the direction of their own life and worried about their children, has serious implications. The task is to help women to turn back or, better still, not to engage in the destructive downward spiral. Much needs to be done to help women to recognise their problems at an early stage, and to make advice, treatment and rehabilitation relevant, accessible and acceptable.

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Life Stress and Post-Partum Psychosis: a Preliminary Report

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This is a preliminary report from a prospective study of the influence of psychosocial stressors on post-natal relapse in women at high risk of psychiatric disorder after childbirth. Forty-three index subjects with a previous history of psychosis or severe depression were compared with 45 pregnant control subjects without any previous psychiatric disorder. After delivery 51% of index subjects relapsed (RDC diagnoses): 28% were categorised as psychotic and 23% non-psychotic. All psychotic relapses were in women with a previous history of bipolar or schizoaffective disorder (46% of this subgroup). Only the non-psychotic post-partum relapses (mostly depressions) were associated with an increased likelihood of a severe life event in the 12 months preceding illness onset.

The relative risk for a woman to be admitted to a psychiatric hospital with a psychotic illness in the first month after childbirth is about 22 times greater than in any of the 24 months preceding delivery; such an admission is 35 times more likely after the first baby (Kendell *et al*, 1987). Rates of admission to mental hospital have remained constant over several decades (Hemphill, 1952; Polonio & Figueiredo, 1955; Murphy, 1982; Stern & Kruckman, 1983). These observations, together with the short delay between childbirth and onset of illness and the early symptoms of perplexity and confusion which are suggestive of an organic disturbance, add some weight to the hypothesis that the primary aetiology of post-partum psychotic breakdown may be in the physiological domain and that psychological and social factors are of secondary importance. A similar conclusion was reached by Hemphill (1952) whose study - 1938 to 1948 - straddled the war years. Having found no difference between rates of mental hospital admission for puerperal illness in peace or wartime, Hemphill concluded: "the war covered half the period under review. During this time there was every combination of bad social conditions - psychological trauma, separation from husband, illegitimacy, bereavement, bombing and housing difficulties. None of these factors, alone or together, appeared to exercise an important influence on the development of mental illness."

Broadly similar generalisations can be made from the results of large epidemiological studies (e.g. Paffenbarger, 1964; Kendell *et al*, 1976, 1981, 1987) in which the main and most consistent associations with post-partum psychotic breakdown were primiparity (two-thirds of all cases), a past history of manic–depressive illness or of post-partum psychosis (recurrence rate >20%) and a family history of manic–depressive psychosis. Caesarian section, prolonged and difficult labour, stillbirth and being a single mother have also been implicated to a lesser and more variable degree. Clearly, the effect of primiparity may be one of either physiology or psychology or a combination: huge changes occur in both domains when a woman has her first child. The possible contribution of obstetric problems to psychiatric breakdown and admission after delivery (e.g. Paffenbarger, 1964; Kendell *et al*, 1987) may be partly or entirely ascribed to an effect of parity. First-time mothers are more likely to experience such problems and they are also at greatest risk of developing a psychotic illness. The increased risk of puerperal admission associated with a stillbirth or neonatal death appears to be limited to non-psychotic illness. The data of Kendell *et al* (1987) indicate that rates of neonatal death in their subgroup of women admitted with a psychosis were identical to those of the community comparison group. Dean (1989) reports that admission to hospital after the loss of a child is associated with depression and not psychosis. In a study she carried out with Kendell (Dean & Kendell, 1981) all women who were admitted after the loss of their baby had a diagnosis of major depressive disorder according to Research Diagnostic Criteria (RDC). Only one factor, absence of a stable partner, appeared to fall into the category of putative social agent. Even here, it is possible that constitutionally or psychologically determined premorbid traits may have explained the breakdown or lack of a stable marital or common-law relationship.

However, Dean & Kendell (1981) have suggested, on the basis of their study of case notes of women with puerperal psychotic illnesses, that stressful life events may play a significant part in the aetiology of these conditions. They found that 82% of women admitted to hospital within 90 days of delivery had long-term difficulties or life events (Dean, 1989). Life stress has been implicated in the exacerbation of symptoms in almost all psychiatric disorders, including those which are believed to have a constitutional component, such as schizophrenia (Birley & Brown, 1970), both endogenous and reactive depressions (Perris, 1984; Cornell *et al*, 1985; Bebbington *et al*, 1988) and mania (Ambelas & George, 1986; Ambelas, 1987; Aronson & Shukla, 1987).

Two studies have systematically investigated the association of life events with the onset of post-partum illness severe enough to warrant admission to a psychiatric hospital. Martin *et al* (1989) used the Life Events and Difficulties Schedule (LEDS; Brown & Harris, 1978) which assesses both life events and ongoing chronic difficulties. In a comparison of events and difficulties in the period from delivery to onset (an average time of four weeks) there was a significant difference between the groups: women who had been admitted with a post-partum depression were twice as likely to have had an event as puerperal controls. This result is remarkably similar to that obtained by studies of the less severe post-partum depressions (see review by O'Hara & Zekoski, 1988).

Martin *et al* also measured life events in women admitted during pregnancy. They found that seven out of eight pre-partum depressions were preceded by a severe event or major difficulty in the 38 weeks before onset compared with nine out of twenty-six women who became depressed after childbirth, and concluded that social difficulties may be less important in the aetiology of the post-partum disorders than in those occurring before delivery. As additional evidence for this view, they reported associations between a number of other psychosocial stressors and depression in pre-partum and post-partum cases. Only two, a lack of a confiding relationship and marked housing problems were associated with post-natal depression. Being single, marital problems, the pregnancy a third or later child, unplanned pregnancy, financial problems and being working class were not. In contrast, such variables were significantly associated with pre-partum depression, suggesting that the raised incidence of provoking agents preceding the pregnancy depressions may indeed have been due to social difficulties.

In another study of post-partum admissions, Dowlatshahi *et al* (1991) using Paykel's life events interview schedule (Paykel *et al*, 1980) compared 33 women admitted to a mother and baby unit within one month of delivery with a group of 33 matched puerperal controls. They found no differences between the two groups on many different analyses of events occurring over a variety of time periods, including the year before delivery until illness onset, the three months before pregnancy, the three trimesters of pregnancy, and the time from delivery to onset. They also looked at a number of psychological variables and again there were no differences between the groups except that women in the index group were more likely to have had a previous psychiatric history.

The results from this study are particularly interesting because here subjects were matched on age, parity, marital status and social class and each of these factors may influence both event rates and psychiatric morbidity. The index group were diagnosed as having a variety of psychiatric disorders: 12 were depressive disorders, 15 were manic or schizoaffective and the remaining six, other diagnoses (ICD-9 (International Classification of Diseases) categories). Eight women (25%) were without partners and 22 (66%) were primiparous. The life-event rate for index and control groups was similar to that reported for depressed women by Paykel *et al* (1980) suggesting that socio-demographic factors may have determined rates in the earlier study and that when such factors are taken into account the effect of life events disappears.

There is always a problem in interpreting findings from retrospective studies because of the confounding effects of the illness itself, and this is especially so when the study involves the reporting of social phenomena such as life events. Moreover, event rates may even be a correlate of a tendency to psychiatric morbidity – people prone to psychiatric illness may have more life events, regardless of whether or not they subsequently become ill (Cornell *et al*, 1985). Indeed, one recent community study has reported elevated rates of life events in the families of depressed patients (McGuffin *et al*, 1988). Secondly, the confounding of demographic and psychological factors with rates of life events means that in many post-natal studies it is difficult to disentangle the independent contribution of variables, or their interacting effects, to post-partum mental illness.

A prospective study of women at high risk of post-partum psychosis

We are carrying out a prospective study of psychosocial stressors in post-partum psychosis as part of a larger project in which many hypotheses, physiological, psychological and social, relating to psychotic breakdown, are being tested. The study is still in progress and preliminary life event findings are reported here.

Method

The subjects are pregnant women with a previous history of severe mental illness who are at high risk of a post-partum illness. Women with a previous episode of bipolar or schizoaffective disorder, according to RDC (Spitzer *et al*, 1978), are categorised as having had a psychosis and those with a previous episode of major depressive disorder as having had a depression. Women with a diagnosis of schizophrenia are excluded. Subjects are referred to the project from hospitals mainly in Greater London. A group of control subjects without any previous psychiatric history has been recruited from the antenatal clinic at King's College Hospital. Assessment of life events and psychosocial stressors is carried out during the pregnancy, prospective to the onset or otherwise of post-natal illness, and subjects who are subsequently categorised as having a post-natal relapse are contrasted with those who remain well, on the basis of predetermined clinical criteria.

Assessment

Clinical and psychosocial assessments were made independently, thus reducing experimenter bias. RDC diagnoses of the woman's previous psychiatric history, psychiatric condition during the 12 months preceding delivery, at the 36th week of pregnancy and from then until six months post-partum, were based on case notes and SADS (Schedule for Affective Disorder and Schizophrenia) interviews at 36 weeks antenatal and six months post-partum respectively, and PSE (Present State Examination; Wing *et al*, 1974) interviews at 36 weeks antenatal and four days, six weeks and six months post-partum.

Interviews for life events, using the methods and schedule of Paykel *et al* (1980) took place at 36 weeks into the pregnancy and covered the 12 months preceding the expected delivery date. The women were again asked about life events occurring since the antenatal interview at six months post-partum.

Results

Diagnosis on relapse

Data are now available from 43 index subjects and 45 controls. No subject was an RDC 'case' from the last two months of the pregnancy until after delivery and all were drug-free during this time. Twenty-two (51%) of the index subjects were categorised as an RDC 'case' during the six-month post-natal follow-up. Of these relapses 12 (28%) were categorised as psychotic (10 mania or hypomania, 2 schizomania) and 10 (23%) as non-psychotic (7 major or minor depressive disorder, 2 panic disorder, and 1 generalised anxiety disorder). Only one of the non-psychotic group was admitted to hospital and she had a major depressive disorder without any evidence of psychotic symptoms. Ten of the psychotic group were admitted. Three (7%) of the control subjects were RDC 'cases', all non-psychotic.

Life events

We have analysed events of marked or severe negative impact (score 1 or 2), probably or almost certainly independent of illness in the 12 months preceding illness onset. Mean onset time for all relapses was seven weeks post-partum and so the comparison period for healthy subjects has been taken as the 12 months up to two months after childbirth. Women who became ill were significantly more likely to have had a severe event in the 12 months preceding onset than other subjects. Of the index subjects who relapsed 11 out of 22 (50%) had an event compared with 4 out of 21 (19%) of those who remained well ($\chi^2=4.53$, $P<0.05$) and 10 out of 42 (24%) of well controls ($\chi^2=4.49$, $P<0.05$).

Table 1 categorises the subjects according to their past psychiatric histories and psychiatric outcome after this delivery. The 'psychosis' group consists of 26 women with a previous episode of bipolar (I or II) or schizoaffective disorder, the 'depression' group, the 17 with a previous episode of major depressive disorder, and normal controls are the 45 women without any previous psychiatric disorder. The denominator in each subgroup refers to the number of subjects in that category who either remained well, suffered a non-psychotic relapse (major or minor depressive disorder, generalised anxiety disorder, panic disorder) or who had a psychotic relapse (bipolar (I or II) or schizomania). Thus, of the 26 women with a previous psychotic illness, 9 (35%) did not relapse, 5 (19%) developed neurotic disturbances and 12 (46%) had a psychotic relapse. Five (29%) of the 17 women with a history of major depressive disorder had a post-partum recurrence but none became psychotic. Three control subjects (7%) became depressed. The numerator in each case refers to the number of subjects in that subgroup who had suffered at least one severe life event in the preceding 12 months.

Table 1
Psychiatric history, psychiatric outcome and proportion of subjects with a severe life event in 12 months preceding onset of illness

	Previous Psychiatric History			
	Psychosis[1]	Depression[2]	Control	Total
Post-natal relapses				
not ill	3/9 (33%)	1/12 (8%)	10/42 (24%)	14/63 (22%)
non-psychotic	3/5 (60%)	3/5 (60%)	2/3 (67%)	8/13 (62%)
psychotic	5/12 (42%)	0	0	5/12 (42%)
Total	11/26 (40%)	4/17 (24%)	12/45 (27%)	

1. RDC diagnoses of bipolar (I or II) or schizoaffective disorder.
2. RDC diagnoses of major depressive disorder.

Only illnesses categorised as non-psychotic (mostly major depressive disorder) were associated with a greater likelihood of the subject having experienced at least one severe life event. Of all women with a non-psychotic post-partum illness, 62% had a preceding event compared with 22% of all women who were not ill ($\chi^2 = 8.10$, $P = 0.004$). The event rate for women with a psychotic illness after delivery (42%) was raised, but not significantly higher than in the total not ill group ($P = 0.16$). All psychotic relapses occurred in women with a previous history of bipolar or schizoaffective disorder. If the comparison is restricted to this subgroup, i.e. those who had a psychotic relapse compared with women with a previous history of bipolar or schizoaffective disorder who were not ill after this delivery, of whom 33% reported an event, then there is virtually no difference in event rate. This is because women with a history of bipolar or schizoaffective disorder tended to have higher event rates, regardless of whether or not they subsequently relapsed, than women with a history of depression, or normal controls.

Initial analyses of the data indicated that certain demographic factors influenced event rates: there was a tendency for first-time mothers and single mothers each to have more life events. To confirm that the differential association of relapse category with life events was not due to demographic factors, we included marital status and parity (primiparous v. multiparous) in a log-linear analysis with life events (presence or absence) and post-natal outcome category (not ill, non-psychotic, psychotic). The interaction between having an event and post-natal illness category remained significant (partial $\chi^2 = 9.62$, d.f. 2, $P < 0.01$).

Finally, the likelihood of an event preceding a non-psychotic illness was similar across all three psychiatric history groups suggesting that when severe life events do contribute to the recurrence of mental illness after childbirth the diagnosis is likely to be major depression.

Discussion

These findings suggest that life events may be significant precursors of non-psychotic post-partum illness, but are less important in the aetiology of the more severe psychotic post-partum disorders. The latter result is similar to that of Dowlatshahi *et al* (1990) who used the same methods to assess life events, and also found no significant association of life events with severe post-partum illnesses in general. Dowlatshahi *et al* also examined life events in the subgroup of women admitted for post-natal depression and found no increased number of events before onset. The increased likelihood of the presence of a 'provoking agent' (life event or difficulty) during the month after delivery in the depressed patients investigated by Martin *et al* (1989) may be an effect of social adversity rather than actual life events, since in their study events were rated as 'severe' if certain associated adverse background factors were also present. For example, not having a confiding relationship significantly correlated with post-partum depression, and this background factor may also have contributed disproportionately to the event rate in the post-partum depression group. Alternatively, it may be that life events are indeed precipitators of non-psychotic post-natal depressions, even those severe enough to warrant hospital admission.

The evidence for a clear contribution of life events to the aetiology of post-partum psychosis is lacking. The factor which is least disputed as important is that of a psychiatric history of manic-depressive psychosis, and the results from our study further support the view that women with a history of bipolar illness are a particularly high risk group. We have yet to examine the cumulative effects of life events and other psychosocial variables such as chronic social difficulties, marital and other relationship problems, being single, and their interactions with relapse rates in this study.

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Women as Perpetrators and Victims of Crime
A Sociological Perspective

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A strong emphasis on individual psychopathology has informed much discussion on female crime, although more recent research has stressed its social setting and influences. Women commit all types of crime, although to a much lesser extent than men, particularly with regard to violent crime. Social and economic marginalisation is a significant factor in female crime. Criminal convictions seem to be more stigmatising for women. In court, women are treated as doubly deviant and their actions are explained in psychopathological terms. Because of the small numbers of women offenders, non-custodial and custodial provisions for them are inadequate. Although men are more likely to be victims of, for example, street crime, women express more fear of crime. One reason for this may be the prevalence of domestic crime committed by men against women (and children) that is underestimated in some surveys.

It may at first sight seem strange to link together the experiences of women both as offenders and as victims of crime. Common sense would suggest that they represent quite different areas of behaviour and of study. Yet in certain judicial practices and in a number of research studies, the role of women in both cases is seen as that of a victim. In particular, court and psychiatric practice have combined to medicalise female criminals and to explain their actions in psychopathological terms (Allen, 1988). Penal policies for women have at times, too, been aimed at women inmates assumed to be either physically or mentally sick or both. Penal practice has not usually succeeded in meeting these aims (Heidensohn, 1975, 1981; Smart, 1977).

Such approaches take away any sense of agency from women; they are depicted as lacking any choice or freedom of will. To see them as helpless and passive in the face of overwhelming psychological forces or hormonal urges which compel them to crime denies them moral responsibility. Not to be able to make choices suggests a lack of self, of full adulthood. In fact women do not play the same parts as victims and as offenders; the picture is more mixed and more complex: there are both some key differences and certain similarities.

The last two decades have been a period of major research and of public interest in women and crime (Heidensohn, 1985; Carlen, 1985, 1988). The findings of these research endeavours give us a clearer, although still partial, image of criminal women and women victims. Earlier generations of studies had emphasised psychobiological aspects of female deviance (Ferrero & Lombroso, 1985; Thomas, 1923; Konopka, 1966; Cowie *et al*, 1968; Gibbens, 1971). More recent work has presented a much more socialised view of women, depicted in social settings, not as isolated individuals, and analysed in sociological rather than psychological terms. The corpus of such work is considerable, but three key areas can be distinguished:

(a) women offenders compared with male offenders
(b) women and men victims of crime and their fear of crime
(c) women's and men's experience of the criminal justice system.

Women offenders compared with male offenders

Female offenders are best described as smaller shadows of their male counterparts. Only 15% of serious offences in England and Wales are committed by women. (All criminal statistics, unless otherwise indicated, are from Her Majesty's Stationery Office, 1989). Most women before the courts are first offenders; few women are recidivists. Women commit all types of offence, but their share of them is very modest and particularly so in violent crimes. Over their respective lifetimes, an average man has a much greater likelihood of being convicted of an offence than a woman. Farrington (1981) estimated that 43% of men, but fewer than 15% of women are likely to be convicted during their lifetimes. Harvey & Pease (1987) calculate that "males are eighteen times more likely to serve a custodial sentence than females". In consequence, women comprise only 4% of the prison population. Their very small numbers have been deemed not to warrant the provision of certain specialised facilities, such as psychiatric prisons or detention centres.

During the 1980s certain changing trends were noted in female criminality both in Britain and in several other industrial nations. Female crime rates rose faster than those for males in several years. (They have fallen more recently, however). Drug-related offences were among the fastest rising category. What had seemed a thinkable proposition in 1970, namely that the 20th-century decline in female imprisonment might lead to its ending by the 21st century, became utopian in the 1980s (Home Office, 1970; Heidensohn, 1975). (All references, unless otherwise indicated, are to *Criminal Statistics*.)

One hypothesis that caught public attention in the 1970s was that 'liberation causes crime'; in other words, that the rise of modern feminism had led to women becoming more like men in everything, including their criminality. The hand that rocked the cradle was now said to be robbing banks (Adler, 1975; Simon, 1975). Statistical analysis does not in practice support such assertions (Smart, 1979; Austin, 1981; Box & Hale, 1983). Women's crime rates had been rising since before the advent of feminism and the women and girls who contribute most to official crime records, those aged 15–18 years and from the lowest socioeconomic groups, are the least likely to have heard of or appreciated feminist thought which has been a very middle-class manifestation. Such theories have also led to studies of alternatives to official crime figures in order to examine whether female crime is under-reported compared with that of males. Victim surveys, self-report studies and scene-of-the-crime accounts suggest that while there is much unreported and unrecorded female offending, there is at least as big an iceberg of male crime (Heidensohn, 1985, 1989). Indeed, it is likely to be even greater since domestic crimes, such as wife beating and sexual abuse of children, have some of the lowest reporting rates of all and are mainly committed by men (Hough & Mayhew, 1983; Stanko, 1988; Hanmer & Saunders, 1984).

Rather than emancipation playing a large part in female crime, it is social and economic marginalisation which emerges as among the most significant factors. In a series of empirical monographs, Carlen (1984, 1985, 1988) has charted the links between poverty, low educational levels and the conventional feminine role (what she calls the 'gender bind'). She notes the short ladder from care to custody for wayward girls who will not submit to discipline and have no economic support. While some of these descriptions could apply to men, women have been particularly vulnerable because they usually carry the responsibility of childcare and have been especially affected by developments in the welfare system in the 1980s.

Criminal convictions appear to be more stigmatising for female than male offenders. Women are more likely to lose the custody of their children and to be regarded as more 'evil' and 'unnatural'; compare the media treatment of the Moors' murderers Ian Brady and Myra Hindley. Several accounts of the effects of conviction and imprisonment show these are particularly damaging for women and girls. Carlen (1984) reports on the adverse attitudes of Scottish sheriffs to women criminals who were mothers (p. 66) and on their propensity to impose custodial sentences on these women. Considerable research has been conducted on the relatively harsh treatment of 'deviant' young women as compared with young men, clearly related to double standards (Chesney-Lind, 1973; Biron, 1981; Webb, 1984). Worrall (1990) interviewed 56 professionals who worked with female offenders in the criminal justice system. She notes their tendency to use a variety of strategies to prevent their clients being publicly stigmatised and humiliated.

Victims of crime and the fear of crime: men and women compared

Women and men differ mainly in degree in their criminality. Men are much more criminal, women more controlled and conforming. However, the sexes vary much more markedly in their experience as victims of crime and still more in their expressed fears of crime. A series of national surveys, pioneered in the US and imitated in most other western nations since the 1960s (Phipps, 1986; van Dijk, 1990; Hough & Mayhew, 1983; Mayhew *et al*, 1989), have highlighted a paradox: it is young men whose lifestyles take them into public houses and street life who appear most likely to be victims of personal violence; yet it is women who express most fear of crime and whose behaviour is altered to the point at which they can be described as enduring a curfew on inner-city estates (Hough & Mayhew, 1984; Middlesex Centre for Criminology, 1990). While overall risk rates for women of street attack may be lower than for men, it is clear that other factors are also involved. Firstly, some crime surveys have underestimated rates of domestic violence: the first British survey questioned women in the presence of their husbands/partners. Secondly, local surveys, especially in inner city areas, produce very much higher victimisation rates for women (Hanmer & Saunders, 1984; Jones *et al*, 1986). Stanko provides a useful survey of findings in this area (1988) and one of the few comparative accounts (1990).

The growing demand for women's refuges, for rape crisis centres and for child abuse helplines all testify to a large, and largely hidden, range of domestic crime in which the perpetrators are mainly (but not solely) male and the victims very often female. That indeed is the key difference in this area: men tend to harm each other in violent attacks; they also attack women and children. Women are very much less likely to harm men.

Results from several studies suggest that fear of crime is a complex issue in which rational understanding of risks may be related to experience. Young women in inner cities are at high risk and very apprehensive. Vulnerability due to other factors such as age, ethnic minority status, poverty, divorce or widowhood and, above all, sex, all compound the problem, making the impact of crime and its associated traumas greater (Hough & Mayhew, 1983; Middlesex Centre for Criminology, 1990). Women's fear of crime may be well founded, although it is in the home rather than on the street that there is the greatest prevalence of crimes.

Experiences of the criminal justice system

As both offenders and victims, women and men have somewhat different experiences of the criminal justice system. Two key issues stand out from current research and debate. Firstly, because women appear relatively rarely before the courts, and also no doubt because the police and the courts are such male-dominated agencies, women offenders are treated as doubly deviant: they have transgressed both the criminal law and social regulation of 'proper feminine conduct'. Thus they may be remanded in custody for reports or be more likely to be placed under supervision than are men (Dell, 1971; Webb, 1984). Indeed, the behaviour of young women in particular is much more likely to be scrutinised and controlled than that of their brothers (Cain, 1989). Allen (1988) has shown, as indicated above, that some women may be more leniently treated – the 'chivalry' hypothesis – because of their sex, but most other research does not confirm this view or is equivocal (Smith, 1988).

Secondly, provision for women offenders in both custodial and non-custodial forms can be described as a Cinderella service: women are 'too few to count' and thus lack, for example, good education and training facilities (Dobash *et al*, 1986) in prison, or pose problems for Intermediate Treatment because of their small numbers (Bottoms & Pratt, 1989). Women offenders, it can be argued, suffer because they are fitted into a system designed to control the much larger and more visible problem of male crime. They are sometimes, however, treated as special cases, either doubly deviant or sick, not criminal (Edwards, 1984). Women as victims of crime do not seem to be treated in this 'special' way; rape victims, while they may remain anonymous, can be subjected to detailed and aggressive cross-examination (Adler, 1987) or imprisoned for contempt for refusing to testify through fear of reprisal. In short, while women offenders are not always treated as rational beings, victims of crime are usually expected to be.

Conclusions

A strong tradition of individual psychopathology has informed much discussion of female deviance. More recent research has emphasised its social setting and influences. The social construction of female victimisation, and women's fears of crime can also be understood in terms of sex roles and the distribution of power and resources in our society.

In considering ways in which crime and fear of it may be reduced, models from both traditions can help form solutions. Clearly there will be cases where individual clinical treatment may be appropriate. For the majority, a public health model is probably much more appropriate. With this one would seek to eradicate poverty and poor housing, and improve educational standards. Empowering women to fight their fears and insecurity through better economic welfare, networks, support groups etc., could reduce both female crime and women as victims.

Crime is not an area of achievement for women: they are notable as its victims, not its perpetrators. The first point is surely something to fight: the skills of the therapists and the support of appropriate welfare services and social policies can be brought to bear on it. The second point is one perhaps to learn from in considering the treatment of the majority of offenders: men.

A note on women, crime and mental illness

For a supplement such as this it is perhaps appropriate to comment on issues relating women, crime and mental illness. To do so fully would require another paper; I shall only try to raise some of the key questions on which research has focused and outline some of its results and further sources.

Are women mad and men bad?

Turk (1969) suggested that being diagnosed as mentally ill was for women a functional equivalent of men being arrested for crime. More women than men are admitted to psychiatric hospitals. In 1981 the female : male ratio for all admissions and all ages was 1.39 : 1 and for first admissions 1.30 : 1

(Busfield, 1986, p. 59). While one in nine men are likely to suffer from a mental illness at some point in their lives, one in six women are. There are, of course, well-known caveats to be attached to this data.

Diagnosis of psychiatric disorder may not be race, class, gender or culture free. Women may be over-diagnosed as sick while sick men are ignored (Chesler, 1972). Illness and deviance are obviously neither functional equivalents nor are they processed in the same way. Moreover, the sex differences in recorded psychiatric disorders are nothing like as great as those in recorded crime.

Are women offenders more disturbed than male offenders?

There is a long tradition of treating female offenders as abnormal, especially those in prison (Thomas, 1923; Pailthorpe, 1932; Konopka, 1966; Gibbens, 1971). Gibbens (1971) certainly found nearly half his Holloway sample suffered from psychiatric disorders. More recently, at Holloway, Turner & Tofler (1986) noted that half their sample of 708 women had some form of psychiatric morbidity, although they included drug users in this group. Posen (1988) reports that 37% of women in her Holloway survey had recent diagnoses of anxiety or depression. While these proportions are high, mental illness is also common among male prisoners. Penal populations are very limited bases from which to generalise to wider groups of offenders as they represent a very skewed sample. It does appear that women react more adversely to prison conditions. More discipline offences are recorded in female establishments; while male suicides in prison are much more frequent, non-suicidal self-injury is relatively frequent among women: in 1987–88 about one-third of the total of such incidents was accounted for by women (Home Office, 1988, pp. 78–79).

Does psychiatry control deviant female behaviour?

Chesler (1972) has suggested that psychiatry is sexist and that it has helped to oppress women by labelling deviant female behaviour as abnormal and treating them repressively. Several writers on crime have used this approach to suggest that deviant women are medicalised and dealt with by an oppressive therapeutism (Edwards, 1984; Iles, 1985). Another strand of feminist thinking sees the social system, rather than the psychiatric profession, as oppressing women and causing their higher rates of mental illness (Oakley, 1982; Brown & Harris, 1978: Eichenbaum & Orbach, 1982, 1985). Allen (1986) has criticised Chesler's work and has also published a study comparing men's and women's treatment by the courts for serious offences (Allen, 1988). She argues that women receive greater lenience because of psychiatric intervention. Busfield (1989) has reviewed both approaches, concluding that there is some merit in each and arguing that both psychiatry and its locus are changing, with a consequent diminution of sexism. "There is plenty of scope for feminist intervention within psychiatry as in other realms of the social order" (1989, p. 361). The symposium on which this supplement was based may be a good example of such an intervention.

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Adult Sequelae of Child Sexual Abuse

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At present there is no consensus of opinion about the short-term or long-term effects of child sexual abuse, although there is a growing body of literature on the subject. Definitions of what constitutes child sexual abuse vary enormously and, even where agreed, include a wide range of behaviours. Most clinical reports are retrospective in nature and based on self-report. Many authors agree that effects can be classified into four general areas, however, emotional/psychological; sexual adjustment; interpersonal relationships; and social functioning. There are considerable implications for treatment of those who have been abused and for the protection of their children.

The debate over the effects of child sexual abuse spans almost a century. It was an issue considered at length by Freud, who came to hold the view that his female patients' accounts of sexual experiences with their fathers were those of fantasy, not reality (Freud, 1962). This view has since been challenged by writers such as Masson (1984). Studies of sexuality in the 1920s by Hamilton (1929), the '30s by Terman (1938) and the '50s by Kinsey *et al* (1953) subsequently addressed this issue. This viewpoint has been reinforced more recently by the women's movement, which has sought to highlight the frequency of sexual victimisation, not only of children, but also of adult women (Herman & Hirschman, 1977; Butler, 1978; Armstrong, 1978). However, other authors have urged that public and professionals alike should give up alarmist concerns about child sexual abuse development (Menninger, 1942; Storr, 1965; Pomeroy, 1968; Farson, 1974) while other writers even argue that children's sexuality needs to be encouraged and developed (Yates, 1978; Constantine & Martinson, 1982). Widespread recognition by professionals of the problems of child abuse is a relatively recent phenomenon. It was less than 30 years ago that Kempe *et al* (1962) described the battered child syndrome, while the vast majority of literature on child sexual abuse has in general come to the attention of professionals only in the past ten years. Although the study by Finkelhor (1979) of 795 college students, showing that one-fifth of females and one in eleven males had been sexually victimised as children is often quoted, a considerable amount of literature from other authors also emerged at this time. Reports have since appeared at an increasing rate.

Methodological difficulties

We know that the incidence of reported abuse cases is increasing, and from these that girls are more commonly sexually abused than boys. We still do not know how large the problem is, nor whether it is truly increasing in size. We also do not know what the long-term effects are. There is under-reporting of abuse and methodological difficulties in the research that has been done. Some literature suggests that there are no ill effects from childhood sexual abuse. Some suggests that the experiences may contribute favourably to psychosexual development (Kinsey *et al*, 1953), or that they diminish the chance of developing psychosis (Rascovsky & Rascovsky, 1950). This is a minority view, and most studies suggest adverse effects in both the short and long term as a result of childhood sexual abuse. Of course, if we can identify a group of individuals sexually abused in childhood but not subsequently suffering from adverse sequelae, we might then learn a considerable amount about those factors which protect individuals and enable them to go through life with resilience. Mrazek & Mrazek (1987) have discussed those characteristics which may be associated with resilience, under the headings of personal characteristics/skills, life circumstances and environmental factors. They make the point, however, that characteristics developed for survival may become maladaptive if overused when the stressor is absent.

Several authors have discussed the methodological pitfalls of research into the effects of child sexual abuse (Mrazek & Mrazek, 1981; Browne & Finkelhor, 1986). The first point that the Mrazeks make is that there is no universal definition of child sexual abuse, and many studies have not differentiated between the widely disparate types of abuse. This is even so in a recent, and otherwise excellent, collection of research studies and is commented on by the editors, Wyatt & Johnson Powell (1988).

The most widely used definition of sexual abuse is that of Schechter & Roberge (1976) which refers to the sexual exploitation of children as:

> "the involvement of dependent, developmentally immature children and adolescents in sexual activities that they do not fully comprehend, are unable to give informed consent to, and that violate the social taboos of family roles."

The nature of the act can be conceptualised as one of four types. *Exposure* - the viewing of sexual acts, pornography and exhibitionism. *Molestation* - fondling the genitals of the child or asking the child to fondle or masturbate the adult's genitals. *Sexual intercourse* - vaginal, oral or anal intercourse, without use of excessive force, often occurring on a chronic basis. *Rape* - vaginal sexual intercourse without consent; it is often associated with threats of, or actual, violence and may occur on an acute basis.

It can be seen that the term 'child sexual abuse' can cover acts from fondling to intercourse; from sexual intercourse between similarly aged adolescents just below the legal age of consent, to sadistic sexual assaults by adults on infants; from single incidents perpetrated by strangers to frequent contacts over many years by family members or well known family friends.

Very often in research studies there is no clarification of such variables as extent of sexual contact, age and developmental maturity of the young child/person, degree of relatedness between victim and perpetrator, affective nature of the relationship, age difference between victim and perpetrator, and length of relationship. In addition there is usually no clarification of such issues as the pre-morbid temperament and development of the child, and other adverse family/background factors such as material deprivation, emotional abuse, neglect, physical abuse/threats, and marital discord/violence. Nor is there information about how the disclosure of abuse is received, nor whether any treatment has been offered, and if so, at what point in time.

Many single case studies have been described. These can give valuable insights and generate hypotheses, but not general principles. What is needed are epidemiological studies; unfortunately these are few in number, or limited in scope, though some good studies are now being conducted and reported (Wyatt, 1985; Russell, 1986; Bagley & Ramsay, 1986; Burnam *et al*, 1988; Mullen *et al*, 1988).

Generally, three types of samples have been used. (a) Children and families seen soon after the abuse has been disclosed or occurred often comprise short-term follow-up studies, conclusions from which may not hold up over time; these populations may be self-selected, particularly if they are seeking treatment. (b) Problematic populations, for example prostitutes (James & Meyerding, 1977; Silbert & Pines, 1981), drug addicts, psychiatric patients (Carmen *et al*, 1984; Oppenheimer *et al*, 1985) and prisoners, especially sex offenders (Groth & Burgess, 1979) have often been studied. There is a problem of accuracy of retrospective recall in order to obtain histories. While large percentages of such populations appear to have been sexually abused in childhood, it is not known what percentage of all sexually abused children go on to have these disorders. (c) College students have been used in many studies and are important contrast groups to studies on disturbed populations. However, these samples are biased in terms of intelligence, social class and motivation and the data collected are retrospective.

Other problems are that few studies have used standardised data collection and outcome measures, and very few have used a control group for comparison. Many studies are too global and lack specificity and accuracy. In assessing outcome criteria, semistructured interviews to explore specific emotions, feelings or attitudes have been used; otherwise a variety of more objective tests have been used. Most studies have used global ratings to exclude severe psychopathology such as personality disorder, neurosis and psychosis, while others have looked at the outward appearances of social and occupational adjustment such as being married and having a job as equating with the absence of problems. The studies of Bagley & Ramsey (1986) and the Tuft's study (Gomes-Schwartz *et al*, 1990) have used a battery of objective measures. However, to test for the specific and diverse sequelae that have been associated with child sexual abuse it would appear that special instruments need to be developed.

It is also necessary to keep in mind that developmentally specific effects that do not persist, or that assume a different form as the individual matures, may be seen among children. Some effects of molestation may be delayed, with difficulties only becoming apparent in adulthood.

The issue as to whether early sexual abuse and later consequences are causally related is not adequately addressed in most studies. Sexual abuse usually occurs in the context of multiple problems and a 'cause and effect' relationship cannot be established unless these additional problems are taken into account. A variety of possibilities exist for explaining the associations between early sexual abuse and later outcome. The first is that the associations are causal ones, even when other problems are controlled for. The second is that sexual abuse must occur in tandem with other stresses in order to produce long-term results. Thirdly, another factor may, quite independently, result in both sexual abuse and long-term problems: likely examples are inconsistent mothering or maternal rejection.

Long-term effects

Emotional/psychological

Depression is the symptom most commonly reported among adults who were sexually abused as children. This link has been demonstrated in community (Bagley & Ramsay, 1986; Mullen *et al*, 1988) and student samples (Sedney & Brooks, 1984). Studies based on clinical samples (Meiselman, 1978; Herman, 1981) have not shown such clear differences in depression between victims and non-victims, perhaps because of the selection of the groups. Both clinical and non-clinical samples have shown victims of child sexual abuse to be more likely to have entertained ideas of self-harm or to have engaged in self-destructive acts (Sedney & Brooks, 1984; and see Browne & Finkelhor, 1986). Bagley & Ramsey (1986), Courtois (1979), and Herman (1981) found that victims had low self-esteem on long-term follow-up. The literature from clinical populations also suggests that victims continue to feel isolated and stigmatised as adults (Courtois, 1979; Herman, 1981; Browne & Finkelhor, 1986).

A self-damaging life-style may involve, certainly in adolescence, running away from home, living rough, and being used by adults. It may lead to an introduction to offending (if only to provide food and clothes for survival), or alcohol and drug abuse. If this pattern is started in childhood or adolescence it may continue, in whole or part, into adulthood. Self-harm appears to be particularly common after the disclosure that sexual abuse has occurred. While scratching or cutting is often to the arms and wrists, there are accounts of girls who have cut other parts of their body, for example legs, abdomen and breasts, even the face, with the possibility of permanent scarring.

Other symptoms commonly reported are anxiety, tension and sleeping difficulties (Sedney & Brooks, 1984; Browne & Finkelhor, 1986; Bagley & Ramsey, 1986). Oppenheimer *et al* (1985) found an association between eating disorders and a history of child sexual abuse. Morrison (1989), in a study of 60 patients with somatisation disorder reported past histories of increased rates of sexual molestation during childhood as compared with a control group of patients with primary affective disorder. An association between pelvic pain and other gynaecological complaints and sexual abuse has also been reported (Gross *et al*, 1980; Bachman *et al*, 1988; Harrop-Griffiths *et al*, 1988). Arnold *et al* (1990) reviewed seven patients with an extensive history of medical or surgical intervention and a past history of childhood sexual abuse. Briere & Runtz (1988) have shown an association of dissociation and somatisation with prior sexual abuse in a sample of university women. Hysterical seizures are claimed to show an association with sexual molestation (Goodwin *et al*, 1979; Gross, 1979; La Barbera & Dozier, 1980). Putman *et al* (1986) have shown a strong association between multiple personality disorder and prior sexual abuse.

Several authors have described, and explained, the long-term impact of child sexual abuse in terms of persisting symptoms of post-traumatic stress disorder (PTSD) (Lindberg & Distad, 1985; Frederick, 1986; Craine *et al*, 1988). Finkelhor (1988) has challenged this view on the basis that the model does not adequately account for all the symptoms, that it only accurately applies to some of the victims, and that it does not truly present a theory that explains how abuse leads to the symptoms noted. Mullen (1990) also argues that, though many years may separate the assault from the later psychiatric problems, there is rarely any history of persistent psychiatric symptoms during the intervening years. Much clinical experience with adolescents suggests that recurrent and intrusive recollections and dreams of past abusive events, with intensification of anxiety, even panic, when exposed to potentially similar situations, are common. So too is guilt, not only for the supposedly seductive role taken by the girl herself, but also for the failure to save her siblings from the same situation.

Sexual adjustment

Almost all clinically based studies show later problems of sexual adjustment (Meiselman, 1978; Herman, 1981; Browne & Finkelhor, 1986). Two non-clinical studies show effects on sexual functioning as well (Courtois, 1979; Finkelhor, 1979), although Browne & Finkelhor (1986) cite a report of no correlation between sexual abuse and sexual adjustment. Finkelhor (1979) devised a sexual self-esteem score to tap possible effects of sexual abuse on feelings and behaviour. Subjects who had been sexually abused as children were likely to have low levels of sexual self-esteeem compared with controls, even when many background variables were controlled for. Females were likely to report that they had often got into awkward sexual situations. Tsai *et al* (1979) in comparing three groups of women found that 'well adjusted' victims and controls were similar on overall sexual adjustment, but that the victims seeking therapy did show a difference.

Many women victims retreat from all sexual experiences, and there are many anecdotal reports of adolescent girls and young women who describe feeling relaxed with males until they start to make even the gentlest of sexual advances – which leads to a flashback to their previous aversive experiences. Other women are able to engage in heterosexual activities but suffer frigidity, vaginismus, etc. Homosexuality has been described as another possible outcome (Grundlach, 1977) though other studies have found no such association (Meiselman, 1978; Bell & Weinberg, 1981; Finkelhor, 1984).

Throughout adolescence, and also into adulthood, there may be an apparent preoccupation with sexual matters, such as increased masturbation, despair regarding sexual urges, promiscuity, prostitution, and early, unplanned pregnancy. Courtois (1979), DeYoung (1982), Herman (1981) and Meiselman (1978) have reported increased sexual activity and promiscuity in incest victims. Browne & Finkelhor (1986), however, reported no differences in this variable and observed that having experienced child sexual abuse only predicted whether subjects would *describe* themselves as promiscuous, not their actual number of partners.

Interpersonal relationships

Problems with interpersonal relationships are widely reported. Women who have been sexually victimised as children often report hostile feelings towards their mothers and fathers (Meiselman, 1978; Herman, 1981; DeYoung, 1982). In addition, victims report fear, hostility and a sense of betrayal in the context of a close relationship (Meiselman, 1978; Courtois, 1979; Browne & Finkelhor, 1986). This lack of a basic trust in others seems to occur particularly if there has been a poor attachment to the mother. Social isolation compounds the problems.

The literature also suggests that women who have been sexually abused are vulnerable to victimisation in later life. Miller *et al* (1978) and Russell (1986) showed that these women are more likely to be raped when adult and Fromuth (1983), quoted by Browne & Finkelhor (1986), showed that female college students are more likely to become victims of coercive sexual experiences. Many sexually abused girls leave home early and become involved with a partner, which often leads to early pregnancy and may well be associated with violence. Because of lack of contact and/or support from their family and their social isolation, they are often unable to extricate themselves from an intolerable situation. Russell (1986) showed that victims were more likely to have physically violent husbands. She and Briere (1984), quoted by Browne & Finkelhor (1986), showed that these women were more likely to have been sexually and physically assaulted by their husbands than non-victim groups.

As already stated, girls who have been sexually abused often enter into early marriage and have children while still young. It is well recognised that they often choose partners who may not only abuse them, but their children too. These women may have a limited ability to detect abuse of their children and difficulty in believing that abuse has occurred when it is disclosed. For these reasons they have great difficulty in protecting their children. Society and professionals often view these women as continuing victims who fail to protect, or turn a blind eye to the abuse of, their children.

Generally, women are not perceived as being active perpetrators of sexual abuse, although there is increasing professional awareness of this problem. This is neither to imply that these women have not been victims themselves, nor that they do not continue to be victims of their past experiences. Finkelhor & Russell (1984) have considered the issue of women as perpetrators, referring to a National Incidence Study of 1981 and the American Humane Association Study. There are considerable methodological problems with these studies, but it is suggested that approximately 20% of boys and 5% of girls who have been sexually abused may have experienced their abuse at the hands of older females. Since sexual abuse of girls is thought to be so much higher than that of boys it means that, in absolute terms, more girls than boys have almost certainly been sexually abused by women. Fehrenbach & Monastersky (1988) reported on 28 adolescent girls (mostly baby-sitters) aged 10–18 years, seen over seven years, charged with sexual offences against children 12 years or younger. Approximately half of the assaults were termed 'rape', involving either oral, anal or vaginal penetration with a finger or object. The other offences involved fondling short of penetration. Approximately 50% of the girls admitted to having been sexually abused themselves, and 20% to having been physically abused. Cavanagh Johnson (1989) described the sexual perpetrations of 13 girls aged between four and 13 years. She found that all had been previously sexually abused and four physically abused. Ten of the girls chose a victim in their family, the mean age of the victims being four years, four months. The average number of victims was 3.5 (range 1–15). Boys were victimised twice as commonly as girls.

The following vignette is of a girl known to the author:

> A was 16½ years of age on referral. She had a considerable history of physical and sexual abuse – from her father and two brothers. She was allowed to babysit for a nearby family. Eventually she was discovered one day by the father of an 18-month-old child that she was caring for, while the mother was at work. The father found what appeared to be a burn on his infant's cheek and the adolescent, stripped from the waist downwards, sitting astride the naked infant on a bed, rocking backwards and forwards. She could give little explanation for what had happened though, on one occasion, said that "I was only doing what my father did to me".

Not all children who have been sexually assaulted become perpetrators, but Powell (1991) did find, in a follow-up study of 143 sexually abused children, that more than 10% became adolescent perpetrators.

Social functioning

Several studies of special populations suggest a connection between child sexual abuse and later prostitution (James & Meyerding, 1977; Silbert & Pines, 1981). On the other hand, Fields (1981), quoted by Browne & Finkelhor (1986), found that, although 45% of the prostitutes in her sample had been sexually abused as children, this did not differentiate them from a comparison group of non-prostitutes matched on age, race and education. An association between child sexual abuse and later alcohol and/or drug abuse has been found (Herman, 1981; Browne & Finkelhor, 1986). Sedney & Brooks (1984) found, in a sample of college students, a low incidence of substance abuse with no significant differences between groups. Girls who have been sexually abused may experience educational difficulties which affect their later vocational opportunites and perhaps the power that they are able to exercise within a working/commercial sphere. Schools play an important role in the lives of children and may provide, on a daily basis, a trusted adult in whom it is possible to confide. It is often found that children and adolescents confide their experiences of sexual abuse to teachers before anyone else.

Contributing factors

There is, as yet, no clear-cut evidence as to which pathogenic factors lead to a negative outcome for child sex abuse victims. The specific causes of the trauma are neither obvious nor universal. However, in their detailed review Browne & Finkelhor (1986) conclude that there are trends in the findings. Most studies indicate that abuse by fathers or stepfathers has a more negative impact than abuse by other perpetrators. Experiences involving genital contact seem to be more serious and the presence of force seems to result in more trauma for the victim. In addition, when the perpetrator is male rather than female and adult rather than adolescent, the effects of the abuse appear to be more disturbing. The more sophisticated studies found no significant relationship between age of onset and degree of trauma, and of all the areas reviewed by Browne & Finkelhor they conclude that there is little consensus on the effect of duration of abuse on impact. There is certainly general clinical consensus that father–daughter incest is the most traumatic type of relationship and that brother–sister sexual activities, provided that they are not accompanied by violence, are less traumatic, as may be abuse by strangers not known to the child or family.

Although child sexual abuse is described as occurring across all social classes, it does seem that whether or not it occurs in the context of other family difficulties and disturbance is important too. Families where there is material deprivation, physical and emotional neglect, marital discord and violence, alcoholism, physical abuse or the use of physical threats, and single-parent households, possibly with partners that come and go frequently, are more likely to produce disturbed children than those who do not experience these problems. If these factors compound the experience of sexual abuse the outcome is likely to be very poor. Conte & Schuerman (1987) found that victims from families seen by social workers as having significant problems in living or showing more indicators of family pathology do worse than those from families without these problems. Jehu (1988) has shown that many previously sexually abused women have grown up in adverse family situations characterised by: marital conflict/disruption; an ineffective/non-nurturing father, physically abusive to his spouse and children and with a history of abusing alcohol; an ineffective/non-nurturing depressed mother.

Finkelhor (1984) has constructed the Sexual Abuse Risk Factor Checklist which has proved effective in identifying children at risk. The eight strongest independent predictors are: having a stepfather, having lived without the mother, not being close to the mother, mother never having finished secondary school, having a sex-punitive mother, no physical affection from father, low family income, and having two friends or less in childhood. Bagley & Ramsay (1986) also found that parental coldness, lack of support, parental separation, and a poor relationship with the mother predicted poor adult mental health, but did not account for all the disturbances in the sexually abused. Wyatt & Mickey (1988) emphasised the importance of family support in alleviating the lasting effects of childhood sexual abuse and Peters (1988) found that the strongest predictor of risk of sexual abuse was lack of maternal warmth while growing up. Controlling for the effects of maternal warmth did not, however, eliminate the significant relationships between abuse experiences and later psychological problems. On the other hand Fromoth (1986) found that the differences between abused and non-abused college students became non-significant once parental supportiveness was controlled for, leaving her to conclude that the Parental Support Scale was a better predictor of later psychological adjustment than was sexual abuse.

It is generally agreed clinically that mothers are often the key in determining prognosis. If the first reaction of a mother is to disbelieve the child and to continue living with the perpetrator while the child goes into care, the outlook is poor. If on the other hand she believes the child, the outlook is better, particularly if she reports the abuse to the authorities, seeks therapy for herself and her child and insists, if necessary, that the perpetrator, not her child, leaves home. Even if the perpetrator's denial is never overcome, the mother and child may be helped to function at a higher level. There is little research looking at trauma as a function of parental reaction, however. The Tuft's study reported by Gomes-Schwartz *et al* (1990) found that when mothers reacted to disclosure with anger and punishment, children manifested more behavioural disturbances. However, the study did not show that positive responses by mothers were systematically related to better adjustment. Similar results have been reported (Browne & Finkelhor, 1986).

The following vignette is of a case known to the author:

> B, a 16-year-old girl, had been sexually abused by her father over many years, this progressing from fondling to full intercourse. She gave evidence against him in the criminal court and he is now serving a prison sentence. She is in full-time care, although with as much contact with her mother as they can both tolerate. She has shown evidence of self-harm, by abusing drugs, overdosing and wrist cutting as well as considerable violence to staff, having broken the nose of one member. In the course of discussing her past abuse and her anger she suddenly said "the central issue for me is that my mother doesn't believe me – and never will. What's more my father's parole date is in 1991 and he'll be going back home to live". This girl will not be able to do so and, furthermore, feels that once her father has returned home she will not be able to visit freely and see her two brothers.

For this girl the disbelief of her mother has seriously compounded her psychological distress.

Factors outside the family appear to be important too. Russell *et al* (1988) showed that Afro-American incest victims reported greater trauma than white victims. Although it appeared that this result arose partly because the Afro-American victims were subjected to more severe abuse in terms of the sexual acts and the force used, the authors also suggest that the trauma of being raised as an Afro-American female in a racist and sexist society may compound the effects of abuse. Stein *et al* (1988) found that abused Hispanics may be at increased risk for many lifetime and current disorders relative to abused non-Hispanic whites.

Some children have already left home, because of their distress, before they disclose. In these cases the responses of others, such as social workers, teachers, doctors, are important. It is not only whether or not they believe the child, but also the subsequent train of events that they might set in motion, that are important. It is very easy for well-meaning professionals to re-create abusive situations by undertaking many and/or insensitive physical examinations and interviews; by removing children precipitously from homes which, with all their faults, the children will have been familiar with from birth; and by placing them in poor-quality substitute care, where abuse may actually be repeated. Unfortunately we have to acknowledge that there is a shortage of good-quality alternative care for children. The Tuft's research (Gomes-Schwartz *et al*, 1990) found that children removed from their homes following sexual abuse exhibited more overall behaviour problems, particularly aggression, than children who remained with their families. However, removal was complicated by factors in the home environment, in particular negative reactions from their mothers.

The following vignette is of a case known to the author:

> C, 16 years of age, ran away from home in her teens because of sexually abusive experiences. She led an increasingly destructive life-style before being taken into care and losing contact with her mother. She had been sexually abused by her father over many years, and could give a vivid description of the hide-and-seek games that preceded full sexual intercourse many years later. When her father left home she was sexually abused by her stepfather, this being full sexual intercourse while she was in bed. She was finally raped at knife-point by her brother. She was clear that this last incident was the most traumatic of all but, when relating her story, added that what made it so terrible was that when she first told her social worker her story was not believed.

This unfortunate girl had suffered an accumulation of traumas, culminating with the disbelief of her social worker.

Conclusion

Extrapolating from recent prevalence studies (Russell, 1983; Wyatt, 1985), it is probable that at least one-third of adult women and approximately half that number of men have had sexual contact with an older person as a child. It is the view of some that sexual abuse is not traumatic or that its traumatic impact has been over-emphasised. However, as evidence accumulates it is apparent that sexual abuse is a serious mental health problem. Non-clinical studies of adults, including random community samples, have found that child sexual abuse victims had identifiable degrees of impairment when compared with non-victims. Although these impairments are not necessarily severe, all the studies that looked for long-term impairment found it, with the exception of Tsai *et al* (1979). The studies identified differences associated with an event that occurred from 5 to 25 years previously.

All studies used broad definitions of sexual abuse, including single episodes and those where no physical contact occurred, and experiences with individuals not related to, or emotionally close to, the subjects. Although these studies indicate higher risk they are not so specific about the actual extent of impairment. Many victims, when evaluated, appear as only slightly impaired or normal. It is possible that some of the impairment is not tapped by these survey studies.

In summary, it appears that in the short term, from one-fifth to two-fifths of abused children seen by clinicians show pathological disturbance (Gomes-Schwartz *et al*, 1990). Studies of adults suggest that under one-fifth of victims show serious psychopathology. While these findings suggest that serious long-term effects are not inevitable, the risk for mental health impairment must, however, be taken seriously and is likely to occur in over 6% of the female population. As Browne & Finkelhor (1986) state, the current priority is to convince policy makers that sexual abuse has serious effects in both the short and long term. These authors suggest that victims may be further harmed by exaggerated claims about the effects of sexual abuse. "It is not possible to maintain two sets of conclusions about the effects of sexual abuse: a dire one for political purposes, and a hopeful one for family members. Thus the presence of both audiences requires that those who conduct and interpret research in this field maintain a posture of objectivity and balance."

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Sexual Abuse, Disordered Personality and Eating Disorders

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Standardised personality assessments were administered to 50 consecutive referrals to an Eating Disorders Clinic. A history of childhood sexual abuse was identified in 30% of patients using a modified version of the SLEI. This rate is comparable with those from other studies. Overall, 52% of the patients were rated as having a personality disorder but a significantly higher proportion of women with a personality disorder had a history of childhood sexual abuse compared with those without a personality disorder (13/26 v. 2/24, Fisher $P < 0.001$). Although in patients with eating disorders no clear causal link between CSA and personality disorder was demonstrated, our findings emphasise the need to inquire sensitively into the sexual history of such patients.

Child sexual abuse (CSA) is now considered to be a common and previously underestimated problem in modern society. Accurate estimation of prevalence rates and outcome is made difficult by under-reporting, different diagnostic criteria (Markowe, 1988), and the reluctance of victims to reveal information even in 'therapeutic settings' (Sheldon, 1988). Freud, in 1895, proposed a role for CSA in the aetiology of adult neurosis in his 'seduction hypothesis', although later he considered these events to be derived from fantasy. Controversy still exists over the traumatic impact, if any, of sexual abuse on its victims (Browne & Finkelhor, 1986; West, 1988).

Recent evidence from both hospital (Bryer *et al*, 1987; Jacobson & Richardson, 1987; Craine *et al*, 1988) and community populations (Burnam *et al*, 1988; Harter *et al*, 1988; Mullen *et al*, 1988) suggests that CSA leads to serious mental health problems. The long-term effects include depression, anxiety disorders, substance abuse, somatisation disorder and long-standing sexual dysfunction (Mullen *et al*, 1988; Burnam *et al*, 1988; Walker *et al*, 1988; Morrison, 1989).

There are now several studies which have found evidence of CSA in patients with eating disorder (Sloan & Leichner, 1986; Oppenheimer *et al*, 1985; Hall *et al*, 1989; Bulik *et al*, 1989).

It was our clinical impression that eating disorder patients who gave a history of CSA also had abnormal personalities. This raised the possibility that the diverse psychopathology reported after childhood sexual abuse may be linked via abnormal personality development. Briere (1984) described a post-sexual-abuse syndrome which has many clinical parallels with the DSM–III (American Psychiatric Association, 1980) diagnosis of borderline personality disorder, and there is some empirical evidence for this (Herman *et al*, 1989; Zanarini *et al*, 1989).

It has long been thought that certain personality traits were associated with eating disorders. Patients with anorexia nervosa have been described as shy, neurotic, introverted, obsessional, overcontrolled, dependent, perfectionists with poor self-image (Strober, 1985; Smart *et al*, 1976; Leon *et al*, 1985), and many have an avoidant type of personality disorder (Piran *et al*, 1988). Gartner *et al* (1989) described borderline self-defeating and avoidant as the most frequently assigned personality disorders in patients with eating disorders. Patients with bulimia nervosa, by contrast, have been described as impulsive and extrovert (Garfinkel *et al*, 1980; Casper *et al*, 1980). Lacey & Evans (1986) have described a subgroup of patients with bulimia nervosa with 'multi-impulsive' personality, arguably a variant of borderline personality disorder. Bulimia nervosa and borderline personality disorder share many symptoms in common and this may account for the high prevalence of co-existing personality disorder in some reports (Pope & Hudson, 1989). The relationship between personality and psychopathology remains uncertain: do personality characteristics predispose to the development of the eating disorder (Bruch, 1973), or do they modify the expression of the disorder once developed?

This study was designed to assess the prevalence of personality disorder and a history of CSA in a consecutive series of referrals to an eating disorder clinic and to test the hypothesis that the two are associated in eating disorder patients.

Method

Fifty female patients diagnosed as having anorexia nervosa or bulimia nervosa according to DSM–III–R (American Psychiatric Association, 1987) criteria consented to enter the study. They were consecutive referrals to the eating disorder clinic under the care of one consultant. It was explained that the purpose of the research was to enhance our understanding of individual differences in patients with eating disorders with a view to improving treatment. Following the usual psychiatric assessment, a standardised personality assessment interview, the Personality Assessment Schedule (PAS; Tyrer *et al*, 1979) was given. When possible, an informant was also interviewed using the PAS. It was stressed to both subjects and informants that the assessment of personality referred to the period before the development of an eating disorder. At a subsequent assessment interview the patient was asked to complete the Sexual Life Events Inventory (SLEI; Oppenheimer *et al*, 1985) in a private room. One of the female interviewers (JT, LMW) was present to guide the patient and answer any queries regarding the questionnaire, and specific follow-up counselling was offered.

The SLEI covers a spectrum of disturbing sexual experiences and systematically elicits details about each one. The definition of CSA is problematic and ranges from narrow legal definitions of incest (West, 1988) to broader criteria including extra-familial perpetrators and sexual acts other than vaginal intercourse (Baker & Duncan, 1985). In this study CSA was defined as: sexual activity involving contact by a perpetrator five years or more older than the victim who was herself aged 16 years or under (after Browne & Finkelhor, 1986). Rape was defined as unwanted sexual intercourse involving force occurring over the age of 16 years.

The PAS is a structured interview schedule with 24 personality attributes rated on a nine-point scale. Cluster analysis of these attributes separates out 13 diagnostic categories of personality disorder which can be further reduced to four major categories:

(a) antisocial group:	sociopathic, explosive, and sensitive-aggressive personalities
(b) dependent group:	passive-dependent, histrionic, and asthenic personalities
(c) inhibited group:	anankastic, anxious, hypochondriacal, and dysthymic personalities
(d) withdrawn group:	schizoid, paranoid, and avoidant personalities.

DSM-III personality disorder diagnoses can also be reached with the PAS by using a modified scoring system. The schedule has been demonstrated as having inter-rater and temporal reliability (Tyrer *et al*, 1979, 1983). Standardisation in the use of this instrument was achieved by the two raters (LMW, LM) using training video and audiotapes, and audiotaping the interviews with both raters agreeing on scoring. Personality ratings were made blind to the history of sexual abuse.

All of the patients were given the following self-report questionnaires: Eating Attitudes Test (EAT; Garner & Garfinkel, 1979), the Bulimic Investigatory Test Edinburgh (BITE; Henderson & Freeman, 1987), The Body Shape Questionnaire (BSQ; Cooper *et al*, 1987) and the Wakefield Depression Inventory (WDI; Snaith *et al*, 1971).

Statistics

Comparisons between groups were made with analysis of variance for continuous data (the BITE and EAT were logarithmically transformed). Fisher's exact test was used for categorical data.

Results

Demographic details

The three diagnostic groups – anorexia nervosa, bulimia nervosa and mixed pattern of illness – were well matched for demographic features (Table 1); as would be expected, the groups with bulimic symptoms had significantly higher scores in the BITE and BSQ and the group with the mixed diagnosis had significantly higher scores on the EAT.

No patients refused to enter the study. All 50 patients completed the SLEI (thus confirming its clinical acceptability – some even wrote that they were pleased to have been questioned on these matters) and were interviewed using PAS. For 35 of the patients an informant was interviewed in addition to the patients.

Table 1
Clinical and demographic features of each of the diagnostic groups, including scores on Wakefield Depression Inventory (WDI), Bulimic Investigatory Test Edinburgh (BITE), Body Shape Questionnaire (BSQ), and Eating Attitude Test (EAT) as well as body mass index (BMI)

	Anorexia nervosa ($n=28$)	Mixed diagnosis anorexia nervosa/ bulimia nervosa ($n=12$)	Bulimia nervosa ($n=10$)
Mean age (s.d.): years	27 (17–51)	24.4 (19–34)	24.3 (19–35)
Mean age at onset (s.d.): years	19 (13–48)	18.3 (15–22)	19.7 (15–25)
Mean duration of illness (s.d.): years	9 (1–30)	6.1 (2–17)	4.6 (1–10)
Mean maximum BMI (s.d.): kg/m^2	21.7 (18–25)	24.2 (20–31)	26 (24–30)
Mean minimum BMI (s.d.): kg/m^2	13.7 (10–16)	15.1 (12–17)	20 (19–28)
Mean score (s.d.) on:			
WDI	18.3 (2–30)	16.7 (5–27)	15.2 (8–28)
BITE	13.6 (1–28)*	26.5 (22–30)	27 (25–30)
BSQ	100 (38–176)	166 (139–193)*	150 (114–174)
EAT	54 (33–82)	72 (46–92)	49.7 (30–78)

*$P<0.001$ (ANOVA)

Table 2
Details of sexual abuse and personality assessments in patients with a history of sexual abuse.

No.	Current age: years	Age at abuse: years	Abuser[1]	Type of abuse[2]	Repeated[3]	Force[3]	Eating disorder[4] (ED)	Rape[3]	Age of onset of ED: years	DSM-III personality disorder	PAS cluster[4]
1	37	15	FF	GF	0	0	AN	+	14	Obsessive–compulsive	Inhibited
2	22	15	FF	GF	+	+	BN	0	22	Borderline/ antisocial	Inhibited
3	30	12	B	GF	+	+	AN	0	13	Obsessive–compulsive	Inhibited
4	19	7	St	GF	0	0	AN	0	15	Obsessive–compulsive	Inhibited
5	33	9	T	GF	0	+	AN	0	32	Dependent	–
		14	FF	GF	+	+					
6	26	5	U	SI	+	+	AN-BN	+	18	Obsessive–compulsive/ borderline/schizoid	Inhibited
		13	Ms	GF	0	+					
7	25	4	St	GF	0	0	AN-BN	+	22	–	Antisocial
		12	Mo	GF	0	+					
		14	St	SI	0	+					
		14	FF	SI	0	+					
		15	FF	SI	0	+					
8	18	5	U	GF	+	+	AN	0	15	Obsessive–compulsive/ borderline/ dependent	Inhibited
		5	C	GF	+	+					
9	30	13	B	GF	+	+	AN	0	14	Passive/ aggressive/ obsessive–compulsive/ dependent	Inhibited
10	34	6	F	SI	+	+	AN-BN	+	17	Borderline/ antisocial	Antisocial
		9	FF	GF	+	0					
11	25	14	FF	SI	0	+	AN-BN	0	23	Borderline	Inhibited
		14	FF	GF	0	+					
		15	FF	GF	+	0					
12	27	14	St	GF	0	+	AN-BN	+	20	Avoidant/ dependent	Inhibited
13	29	10	F	GF	+	+	AN-BN	+	18	Antisocial/ borderline	Antisocial
		13	FF	GF	+	+					
		14	FF	GF	0	+					
14	30	9	FF	GF	0	+	AN-BN	+	17	–	–
15	24	13	F	GF	+	0	BN	0	18	–	–

1. B = Brother; C = Cousin; F = Father; FF = Family Friend; Mo = Mother; Ms = Stepmother; T = Teacher; St = Stranger; U = Uncle.
2. GF = genital fondling; SI = sexual intercourse.
3. + = present; 0 = absent.
4. AN = anorexia nervosa; BN = bulimia nervosa; AN-BN = mixed diagnosis.

Sexual abuse

Fifteen patients (30%) were found with a history of CSA and details about this are given in Table 2. Fourteen patients had been raped (seven of these had also been abused as children).

Personality disorder

Twenty-six patients (52%) were rated as having a personality disorder in addition to their primary diagnosis. The personality types are variable and are shown in Tables 2 and 3. Thirteen of the 26 patients with a personality disorder had been sexually abused during childhood. A significantly higher proportion of the women with a personality disorder had been abused compared with those without a coexisting personality disorder (13/26 v. 2/24, Fisher $P<0.001$). In contrast there was not an increased proportion of women with a personality disorder in those who had been raped (9/26 v. 5/24, NS). Only two patients sexually abused as children had no personality disorder.

A comparison of the clinical features in these four subgroups – women with a personality disorder who were sexually abused in childhood, women with a personality disorder without childhood abuse, women without personality disorder or childhood sexual abuse and women with childhood sexual abuse but no personality disorder – is shown in Table 4. There were no differences between these groups. Those with a coexisting personality disorder (with or without CSA) had a significantly longer duration of illness (8.9 years (s.d. 3.4) v. 5.6 years (s.d. 2.7) $P<0.05$; 95% CI −0.23–7.11) than those without a personality disorder.

Table 3
Personality assessments in patients with diagnosis of personality disorder but without history of sexual abuse ($n=13$)[1]

No.	Current age: years	Eating disorder[2] (ED)	Age of onset of ED	DSM-III personality disorder	PAS cluster
1	18	AN	16	Avoidant	Inhibited
2	23	AN-BN	19	Borderline	-
3	25	BN	16	Borderline/ antisocial	Antisocial
4	24	AN-BN	18	Borderline/ avoidant	Inhibited
5	18	AN	16	Obsessive-compulsive/ avoidant	Inhibited
6	29	AN		-	Inhibited
7	31	AN	12	Obsessive-compulsive	Dependent
8	20	AN	18	-	Inhibited
9	22	AN	13	Obsessive-compulsive/ dependent/ avoidant	Dependent
10	39	AN	20	Obsessive-compulsive/ paranoid	Inhibited
11	33	AN	32	Dependent	Inhibited
12	26	BN	23	Avoidant/ borderline	Antisocial
13	35	BN	25	Dependent/ avoidant	Inhibited

1. For 22 patients without history of sexual abuse there was no diagnosis of personality disorder.
2. AN = anorexia nervosa; BN = bulimia nervosa; AN-BN = mixed diagnosis.

Discussion

We have shown that 30% (15/50) of the patients attending an eating disorder clinic have a history of CSA. This is in broad agreement with the findings of previous studies; Oppenheimer *et al* (1985), using the same instrument, found the figure to be 29.5%. Hall *et al* (1989), using broader criteria for sexual abuse, found that 42% of their eating disorder patients gave such a history. Gartner *et al* (1989), looking specifically at bulimic women, found that 34% had been sexually abused or had a sister who had been sexually abused.

Only 3/15 had been abused by unknown perpetrators. Although Calam & Slade (1989) speculated that anorexia nervosa would be more common in those with intrafamilial abuse, there was no evidence to suggest specificity between the perpetrator and form of eating disorder.

The association between CSA and rape in adult life, found in 50% of the rape victims in this study, is also in keeping with other studies (Russell, 1986; Miller *et al*, 1978).

Fifty-two per cent of the patients in this study had a diagnosis of a personality disorder in addition to their eating disorder. This finding is in keeping with other published studies (Hudson *et al*, 1983; Levine & Hyler, 1986). It is less than the 87%–97% of anorexic patients with an associated personality disorder reported by Piran *et al* (1988). However, their study differs from ours in making the personality

Table 4
A comparison of the clinical features of the four subgroups, including scores on Wakefield Depression Inventory (WDI), Bulimic Investigatory Test Edinburgh (BITE), Body Shape Questionnaire and Eating Attitude Test (EAT), as well as body mass index (BMI)

	Sexual abuse + personality disorder ($n=13$)	No sexual abuse + personality disorder ($n=13$)	Sexual abuse + no personality disorder ($n=2$)	No sexual abuse + no personality disorder ($n=22$)
Mean age (s.d.): years	27 (18–37)	26 (18–39)	(26–30)	26 (17–51)
Mean age at onset (s.d.): years	18.1 (13–32)	17.7 (12–25)	(17–23)	19.6 (13–48)
Mean duration of illness (s.d.): years	9.1 (1–23)	8.3 (1–19)	(3–13)	5.6 (1–30)
Mean maximum BMI kg/m^2	24 (20–31)	23.4 (20–30)	(23–24)	22.4 (18–28)
Mean minimum BMI kg/m^2	14.7 (10–20)	14.7 (11–19)	(16–17)	15.7 (10–28)
Mean score on:				
WDI	23.8 (18–30)	17.2 (8–30)	(13–17)	18.5 (8–29)
BITE	19.9 (5–29)	15.2 (5–27)	(24–25)	23 (1–30)
BSQ	123 (38–173)	120 (62–189)	(151–174)	128 (65–193)
EAT	63.4 (45–91)	54.2 (40–78)	(43–55)	60 (30–92)

diagnosis on clinical grounds rather than using a standardised instrument. All of these studies, including our own, suffer from the problem that although there is an attempt to assess personality before the eating disorder began, this is inevitably coloured by state effects.

In this study those with a personality disorder had a longer duration of illness, which suggests that this confounding effect is prominent if the length of recall is increased, although the converse (i.e. that a personality disorder alters outcome) may be true.

We have confirmed our clinical impression that eating-disorder patients with a history of CSA often have an associated personality disorder (13/15 patients). The aetiological and clinical significance of this is not clear. Hitherto, no link has been made between personality disorder and childhood abuse in eating disorder patients. In contrast there was no evidence that personality disorders were more common among victims of rape. One could speculate that sexual abuse is more damaging to a developing personality than to an integrated adult one.

The numbers in this study do not allow analysis of the individual personality types. Seventy percent of the abused patients and 61% of the non-abused patients with a diagnosis of a personality disorder fall into the inhibited group.

Childhood sexual abuse is clearly not a prerequisite for the additional diagnosis of a personality disorder in these patients, but a history of abuse makes it significantly more likely. This link with sexual abuse could be direct or could arise from the more general neglect common in families in which abuse occurs, or conversely those women with a personality disorder may be more vulnerable or more likely to report previous adverse experience. There is no clear evidence that CSA results in a specific clinical picture or personality disorder. However, within the abused group all patients subjected to repeated severe abuse had a mixed anorexic-bulimic psychopathology (a known poor prognosis group) and these patients all fell into the borderline/antisocial personality diagnostic category.

To conclude we have shown that patients with eating disorders who have been sexually abused in childhood are more likely to have a personality disorder than those without a history of abuse. We have not been able to demonstrate a clear causal link in that many eating disorder patients have not been abused and yet also have a personality disorder diagnosis. Personality disorder may be the final common pathway of a variety of developmental factors of which childhood sexual abuse, although important, is only one. If personality disorder is found to be associated with poor compliance and outcome it will be interesting to see if this is related to the personality disorder *per se* or to childhood sexual abuse.

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Gender Differences in Carers of Dementia Sufferers

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Recent research shows that the demands of the caregiving role are experienced differently by men and women. Both the subjective and the objective strain and burden appear to be greater in female carers of dementia sufferers, and factors that influence this include differences in role expectations and coping strategies. These findings have implications for the provision of services for dementia sufferers and their carers.

In recent years the development of community care has focused attention on the informal carers of people with psychiatric disorders. A major challenge in this area is the rapidly growing number of dependent elderly people with a progressive decline in mental functioning, arising from the various forms of dementia. Approximately five in six people with dementia live in the community supported by an immediate relative or friend, who can experience considerable burden or strain (Cantor, 1983).

According to the Equal Opportunities Commission Report (Charlesworth *et al*, 1984) women provide most of the care for all categories of elderly disabled people in the UK including those with dementia. In the USA 72% of all caregivers are women (Stone *et al*, 1987). Studies of families of dementia sufferers suggest that the primary source of support follows the principle of substitution in caregiving, with family members providing care in serial order rather than as a family unit. Thus the burden of care falls upon a single household member, usually a woman who is either the spouse or an adult child. Because of this imbalance it has been argued that particular attention should be devoted towards women's experience of caring and their needs. The mental and physical strain of looking after people with dementia has been investigated in some detail and indicates that carers of dementia sufferers experience a range of problems stemming from the practical and emotional burdens of caring. As will be discussed below, women carers appear to be more vulnerable to stress and strain, not least because women are more closely involved in the caregiving process (Morris, R. G., *et al*, 1988).

A key feature of caring for a person with dementia is the progressive decline in the relationship with that person, associated with the cognitive deterioration of the dementia sufferer (Morris, L. W., *et al*, 1988). Typical of the stresses faced by carers are a reduction in financial income, social isolation, and the everyday burden of nursing somebody with a low level of self-care and reduction in daily living activities. The impact of caregiving depends on a range of other factors, such as the level of effective support received from other family members and friends and the carers feeling of control over their situation (Morris *et al*, 1989). The experience of women carers differs from that of men for a variety of reasons. This includes the manner in which societal expectations may determine sex-role behaviours, the different coping strategies adopted by women, and patterns of family interaction. The factors that differentiate male and female carers will be discussed below after reviewing the physical and emotional impact of caregiving.

The impact of caregiving

Much of the recent research on carers of dementia sufferers has followed the distinction originally made by Grad & Sainsbury (1965) between '*objective*' and '*subjective*' burden. Objective burden refers to the practical impact and daily hassles of caregiving such as the physical burden of care, changes in the daily routine, and changes in employment and health. Subjective burden refers to the carers emotional reaction and perception of strain, including morale, anxiety and depression. Gender differences in objective burden are illustrated by the finding that daughter carers are more likely to share accommodation with the dependent relative, which means coping with increasing dependency for a longer period and being more readily 'available' throughout a 24-hour day (Charlesworth *et al*, 1984). Co-resident women carers have also been found to be less willing to go out of the house and leave the dementia sufferer unattended. As a result, female carers tend to experience restrictions on their leisure time, giving up their own social activities more easily and also refraining from seeking employment outside of the home because of their caregiving responsibilities (George & Gwyther, 1986).

The objective burden of caring is also reflected in the health functioning of carers. Haley *et al* (1987)

Table 1
Summary of studies investigating gender differences in subjective burden in carers of dementia sufferers

Study	Measure	Outcome
Global ratings		
Gilleard *et al* (1984)	General Health Questionnaire	Women consistently higher level of 'caseness' in three studies
Gilhooly (1984; 1986)	OARS (Older Americans Resources and Services) 'mental health' scale	Correlation between sex and psychiatric symptomatology; women higher level
	Kutner Morale Scale	Correlation between sex and morale; women higher level
Anthony-Bergstone *et al* (1988)	Brief symptom Inventory	Older women elevated on depression, anxiety, hostility; younger women elevated on anxiety and hostility
Pruchno & Resch (1989)	Hopkins Symptom Checklist	Women complain more of headaches, nerves, dizziness, inertia, perspiring, heart palpitations, sleep problems
Ratings of depression		
Fitting *et al* (1986)	Minnesota Multiphasic Personality Inventory	Higher depression in women
	Wiggins Depression Scale	Higher depression in women
Moritz *et al* (1989)	Centre for Epidemiologic Studies Depression Index (CES-D)	Cognitive impairment in spouse correlates with depression in women only
Pruchno & Resch (1989)	CES-D	Higher level of depression in women

reported that a sample of 44 primary carers of dementia sufferers, the majority of whom were women (72%), rated their health as poorer overall than a control group of non-carer subjects. They also had more chronic illnesses, assessed using the Health Status Questionnaire, and reported a greater number of recent visits to doctors and prescribed medications. Ill-health was attributed both to the stress of caring and to the physically demanding task of nursing, often involving heavy lifting and complete responsibility for household chores. An extreme example of this is the account given by Haley *et al* (1987) of a women carer who died of a heart attack following a period of excessive physical activity associated with caregiving. More recently, Pruchno & Resch (1989) made a direct comparison of the physical health of male and female elderly carers of dementia sufferers with elderly people who were not carers. Carers reported higher levels of chronic conditions overall, but women carers were more likely than male carers to report their health as poor and to report hypertension and arthritis. Again, these changes could be attributed to differential levels of stress as a result of the person's physical and psychosocial environment (Solomon, 1984).

The level of subjective burden is reflected in the psychological well-being of carers, which has been assessed using measures of strain, morale, anxiety and depression (Morris R. G., *et al*, 1988). Studies that have investigated gender differences suggest that subjective burden is higher in women, although the degree of increase varies between studies (see Table 1). Gilleard *et al* (1984) investigated 'caseness' of psychiatric disorder using the General Health Questionnaire, finding that women were consistently more likely to score higher than the threshold for 'caseness' than male carers. The same result was obtained by Gilhooly (1984; 1986) using the 'mental health' scale of the OARS Multidimensional Functional Assessment Questionnaire, with female carers showing greater psychiatric symptoms. Similarly, Fitting *et al* (1986) found that wife carers had significantly higher scores than men on several measures of depression and distress derived from the Minnesota Multiphasic Personality Inventory and the Wiggins Depression Scale.

One problem with these comparisons is that the prevalence of emotional disturbance is higher in women in general. Few studies have made a direct comparison between the mental health status of carers in comparison to non-carers. Pruchno & Resch (1989) measured the level of depression in carers of Alzheimer's disease sufferers and non-carers using the 20-item Centre for Epidemiological Studies Depression Index (CES-D). They found that carers, both male and female, consistently scored as more depressed on the CES-D than did a community sample. However, the level of depression rose more sharply for female carers and the mean level (18.9) exceeded the cut-off score of 16, defined by Husaini *et al* (1980) as indicating 'possible depression'. The presence of psychiatric symptoms was also investigated by Pruchno & Resch (1989) using the Hopkins Symptom Checklist, revealing that female carers were more likely than male carers to complain of somatic symptoms, as shown in Table 1.

Moritz *et al* (1989) used the CES–D scale to investigate a sample of 318 spouse pairs drawn from a representative sample of non-institutionalised elderly subjects. They correlated the level of depression in one of the partners against a measure of cognitive impairment (ie. dementia) in the spouse. In both male and female subjects the degree of depression increased with the level of cognitive impairment, but female subjects were more depressed overall. Despite this there was no difference between sexes in the degree of depression in the spouses of more severely cognitively impaired subjects. Anthony-Bergstone *et al* (1988), using the Brief Symptom Inventory, compared the scores of carers of dementia sufferers with normative data on different features of psychiatric symptoms. The greatest amount of symptoms occurred in elderly women carers (over 60 years), who differed significantly from normative scores on the obsessive–compulsive, depression, anxiety, hostility and psychoticism subscales. This contrasts with elderly men who only differed on the hostility subscale. With younger women carers differences occurred on the obsessive–compulsive, anxiety and hostility subscales, while there was no difference between younger men and the normative population on any of the subscales.

Taken overall, it appears that women carers are more likely to experience emotional problems over and above the baseline levels expected in the normal population, although it should be noted that when the measure of burden is more directly related to the specific impact of looking after the dementing person (e.g. the question 'Do you ever feel frustrated by the person?' or 'Do you feel angry about your interventions with your spouse?'), gender differences are not always found (Fitting *et al*, 1986; Zarit *et al*, 1986). One possibility is that in female carers emotional stress is more likely to have a more general impact outside of the caregiving context, affecting the whole of the person's well-being, whereas for male carers the stress has a more compartmentalised and less global impact.

Gender differences in role expectations

The preponderance of women carers has been noted above, with estimates of the proportion of women carers varying from approximately 70% to 80%. Part of the imbalance can be explained by the greater number of men who are married, and who are thus more likely to have a spouse who can act as a carer (Shanas, 1980). Another reason is thought to arise from the different life experiences and socialisation patterns that men and women experience (Finch & Groves, 1983). Women carers, especially elderly spouses, were raised in a period in which women were socialised to be more family orientated and take on a nurturant role. It has been argued that the role of carer in later life is more readily assumed as an expansion of the traditional responsibilities of a wife or daughter (Treas, 1977).

To some extent the 'socialisation' explanation is supported by studies of carers. For example, Horowitz's (1985) study of son and daughter carers of the frail elderly found that while women tend to aid their dependent parents by help with transportation, meal preparation, errands, shopping and personal care, men tend to help with decision making and personal assistance. Similar results have been found with son and daughter carers in a study by Stoller (1983). However, other studies indicate that the level of caregiving involvement is approximately equal among men and women carers, particularly in carers of dementia sufferers. In her study of 15 spouse carers of dementia sufferers Miller (1987) found that there was no difference between men and women in terms of help given with daily living tasks. More recently, Pruchno & Resch (1989) reported that wife carers of Alzheimer's disease sufferers give the same amount of help in activities of daily living as husband carers, although the latter received more help from other people. Another study of spouse carers of predominantly dementia sufferers by Barusch & Spaid (1989) used a 37-item index of caregiving tasks and found that men reported performing an average of 27 tasks in the month before interview, while women reported performing an average of 23 tasks. Men reported performing significantly more tasks concerned with communication, mobility, hygiene, dressing and feeding.

An alternative perspective on the caregiving role is the aspect of 'being in charge of' or 'managing' another person. Miller (1987) has argued that caregiving can be seen as an extension of the male role as authority figure at home or in work rather than an extension of the nurturing role. The meaning of home for retired men has received little attention or study but there is some suggestion that men transfer the scheduling and task-orientated approach from work. Male caregivers appear to be at ease in taking responsibility for the instrumental aspects of care. Conversely, Miller (1987) reported that women caregivers found it particularly hard to assume an authority position over another adult, especially if they had been used to seeing their husband as an authority figure in the marriage. She recounts that female spouse carers had difficulty assuming responsibilities for finances and instructing their husbands what to do. The pattern of dominance in the relationship has been shown to be important, such that the greater the dominance of the dementia sufferer the more likely the relationship will break down (Bergmann *et al*, 1984).

A range of other factors can be seen as influencing gender differences in attitudes to caregiving. Firstly, women have been affected by changing demographic trends with more of them entering the workforce. Middle-aged women, in particular, may face the competing demands of the immediate family, job responsibility and caring for a dependent parent. The role conflicts this entails has led to the concept of the 'woman in the middle' where conflicting demands lead to ambivalence in the carer. Ambivalence is illustrated by Whittick's (1988) comparison of daughter carers of dementia sufferers with mother carers of children or adults with learning difficulties. She found that the degree of role conflict, family disruption and resentment concerning the caregiving role was significantly greater in the daughter carers. There was also a corresponding decrease in satisfaction and positive feelings towards the dementia sufferer and greater willingness to accept institutional care.

Another related factor is the developmental change in sex-role differences during middle age and later life as proposed by Gutmann (1987) and by Eichorn *et al* (1981). Women can become more instrumental and assertive as they grow older while men can become more nurturant and expressive. Strain may be compounded in middle-aged women carers who are in the process of relinquishing child-rearing responsibilities and plan to take more control of their lives. Likewise, wife carers may view their later years as a time for personal growth and opportunities and resent becoming carers of their husbands (Zarit *et al*, 1986). Seen in this light the caregiving role would be more in line with the needs of men, with women experiencing greater emotional distress as a result (Gutmann, 1987).

This may help to account for Fitting *et al*'s (1986) finding that male spouse carers were much more likely than their female counterparts to report an improvement and less likely to report a decline in their marital relationship since the onset of the dementing illness. Thus the new, challenging caregiving role may be suited developmentally to the needs of some male carers. Fitting *et al* (1986) consider alternative notions, such as male carers being more likely to experience positive feelings from 'repaying' the wife for past nurturing, or from an atoning sense of guilt, where the carer recognises his own responsibility for a previously unhappy relationship. In connection with this, Husband (1987) found that the association between the quality of the past relationship and current levels of strain only existed in female spouse carers. Again, this suggests that male spouses may be buffered from the impact of caregiving, even for a person with whom there has been a poor relationship in the past.

Coping styles and effectiveness

Research into the area of stress indicates that the impact of a stressful experience is influenced by the way people interpret the situation and by the coping strategies they use (Lazarus & Folkman, 1984). In middle-aged women who are carers of dementia sufferers, Pett *et al* (1988) found that the highest levels of burden were reported in women who tended to use regressive and avoidant-evasive coping strategies. Investigations of gender differences in coping strategies generally indicate that women use a greater variety of styles than men, but that women are more likely to use 'avoidance coping', while men tend to describe themselves as more 'active' copers who use more active mastering in their coping responses (Billings & Moos, 1981; Siegler & George, 1983).

There is evidence that women carers of dementia sufferers are initially more emotionally involved than men carers, while men tend to distance themselves emotionally and adopt an instrumental approach to daily problems. A follow-up of husband and wife carers by Zarit *et al* (1986) indicates that after two years wives change their coping style to that of men, with a corresponding decrease in the level of subjective burden. Gender differences in the approach to the behavioural changes of the dementia sufferer are illustrated by the manner in which carers interpret the disease process. Miller (1987) found that wife carers tend to explain their husband's behaviour in terms of changes in the relationship with their husbands, often using the analogy of taking care of a child. In contrast, husband carers referred to problems in the mind of the person as an explanation of the behavioural changes, attributing this specifically to the disease process.

Barusch & Spaid (1989) explored the way carers cope with caregiving problems using a coping inventory which outlined different areas of problems. If a carer reported a problem, they were asked to describe the way they coped with it and how effective their own coping strategy had been. Women carers tended to report feeling more angry, having arguments with their spouse and worrying about financial difficulties. In each case, women tended more frequently to feel that they failed to cope with the situation, whereas men took action to change the situation or used cognitive restructuring to reduce the impact. Men thought they failed to cope in situations where they felt the spouse was more dependent than necessary and made excessive demands on their energy. Men reported feeling greater effectiveness in coping with care management problems, financial problems and personal/health-related problems while women reported coping more effectively with personal/psychological problems.

Discussion

Several findings from the studies reviewed in this article have implications for professionals working with carers. Even allowing for the greater prevalence of emotional problems in women, the level of subjective burden or strain appears to be greater in female carers of dementia sufferers. Although the women have traditionally been seen as carers this can often be a source of conflict in women who either wish to relinquish the caregiving role or who, as in the case of middle-aged carers, may face the competing demands of their immediate family. Women appear to have a more intimate relationship with the dementia sufferer, generally feel less confident in coping with the role of carer and take longer to distance themselves from the dementia sufferer emotionally.

In line with these findings is the higher level of expressed emotion (EE) in women carers, with an increased number of critical comments directed towards the dementia sufferer (Gilhooly & Whittick, 1989). Higher levels of EE in carers or dementia sufferers have in turn been shown to be associated with greater use of maladaptive coping strategies and higher levels of strain (Bledin *et al*, 1990). Distancing emotionally and compartmentalising the stress of caring may be effective strategies, preventing the carer from becoming overwhelmed by strain. Male carers are more likely to maintain other interests and relationships and more readily 'forget' the situation when away from it and are thus less likely to experience pervasive strain (Husband, 1987).

Overall the demands of the caregiving role are experienced differently by men and women and more attention should be paid to this in working with carers. Although at present carers are predominantly women, the traditional view of caregiving as a woman's domain should not go unchallenged, particularly as there is evidence that the caregiving role is more synchronous with the needs of men. The Equal Opportunities Commission report on carers and services (Charlesworth *et al*, 1984) indicates that male carers are more likely to receive home help, meals on wheels, rehabilitation/assessment and long-term care. Community nursing was the only service that was provided equally to both groups of carers. In contrast, preference for community care versus institutional care has been found to be equivalent in male and female carers (Gilhooly, 1986). Levin *et al* (1989) confirm that services are often disproportionately received by male carers, but in part this may relate to current services being better orientated to male needs (e.g. in relation to domestic help); indeed Levin *et al* (1989) reported that the home-help service was effective in assisting male, but not female, carers to continue looking after the dementing person at home over a one year follow-up. In the light of recent research, the current assumptions about stresses and strains in different groups of carers may need to be modified with a greater understanding of how gender differences interact with models of service delivery and community care.

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Sex Differences in Service Usage in Long-Term Psychiatric Care
Are Women Adequately Served?

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There is a paucity of research concerning service usage and needs of female long-term psychiatric patients. A series of studies comparing the provisions for chronically mentally ill men and women in a south London community-focused rehabilitation and continuing care service indicate marked differences in the services received by men and women, and raise questions concerning whether the needs of female patients are adequately served. As a group the women had been in contact with services for longer, had received less intensive input from services, and it appeared that the services had been less responsive to their changing needs. Among those in high contact with the services, the functioning of men and women did not differ, yet women were over-represented in workshops designed for those functioning at a lower level. Women over 45 years of age seemed to be particularly badly served by the organised activities offered.

The last 20 years has seen an increase in attention to gender issues in mental health. There has been much consideration of women's gender-specific treatment needs and service usage in primary care and acute psychiatry (e.g. Gove & Tudor, 1973; Chesler, 1974; Skegg *et al*, 1977; Howell & Bayes, 1981; Briscoe, 1982; Cooke & Ronalds, 1985). Chronically mentally ill women have, on the other hand, received relatively little attention (Test & Berlin, 1981). Recently, there has been some discussion of the gender-specific treatment needs of these women (Test & Berlin, 1981; Bachrach, 1984, 1985; Bachrach & Nadelson, 1988), but there remains an extreme paucity of empirical research concerning their service usage and needs. Without such information it is impossible to assess what services this group are receiving, what the problems might be, and how services might be extended and improved. The purpose of this paper is to report data on service usage by chronically mentally ill men and women from studies carried out in a community-focused rehabilitation and long-term care service in south London.

The District Services Centre (DSC) at the Maudsley Hospital, London, provides the focus of rehabilitation and continuing community care for long-term patients in a poor inner-city catchment area with a population of 120 000. Since its inception in 1981 the service has operated without traditional long-stay wards. All those patients who would formerly have resided in such wards are now cared for by the DSC and its associated 'hostel ward' for 14 severely disabled 'new long-stay' patients (Wykes, 1982). The service looks after approximately 350 long-term patients, 90% of whom, at any one time, live in the community. There are a total of 25 'new long-stay' patients who have been resident continuously in the hospital for more than one year. Some beds are provided for short- and medium-term admission (one night to several months) of long-term psychiatric patients who require periods of in-patient care.

The amount of support required by patients varies both across individuals and within any one individual across time. This support is offered flexibly depending on the individual's current level of need, and can range from in-patient care, through day-care, to infrequent out-patient or domiciliary contact. For all patients, there is no time limit on the support they receive from the service.

The services offered by the DSC include: (a) individual help from a variety of professionals (psychiatrists, psychologists, nurses, social workers, and occupational therapists) both within the DSC and in patients' own homes; (b) medication; (c) meals; (d) groups run by members of staff; (e) recreational activities; (f) a place where patients can meet other people; (g) liaison with, and support for, others involved in the patients' care (families, hostels, day centres, etc.); (h) help with managing money and paying bills; (i) three industrial and one clerical workshop; (j) classes in such things as self-care, cookery, literacy, art and community skills; and (k) in-patient residential facilities.

While each patient has an individual programme tailored to their needs, there has been no explicit consideration of the gender-specific needs of female patients in either the planning of services or their delivery. It has generally been assumed that the service operates equally well for women and men, and that both make similar use of the facilities offered. However, data from two studies conducted between 1984 and 1987 suggests that this may not be the case.

Study 1: a census of the patient population in 1984 and 1987

In 1984 and 1987 a 'one day census' of the patient population was conducted; that is, details were obtained on all those patients 'on the books' on the census days. In both 1984 and 1987 the proportion of men and women in the population was identical: 59% men and 41% women on both occasions. There were also three areas of marked difference in service usage.

Duration of contact with the service

The DSC had been open for 33 months at the time of the 1984 census and 69 months at the time of the 1987 census. In 1984 about half (53%) of male patients compared with nearly three-quarters (71%) of female patients had been in contact with the service since it was established. The mean length of stay for women was 28.6 months (s.d. 8.42) and for men was 23.1 months (s.d. 11.6). In 1987 the picture was very similar: 35% of the male patients had been in contact with the service since it was set up as compared with 55% of the female patients. In 1987 the mean duration of contact with the service was 56.5 months (s.d. 20.4) for men and 61.9 months (s.d. 15.1) for women. Thus it appears that women stay longer within the service.

Level of contact with the service

For the purposes of the census, patients were divided into three groups in terms of their contact with the service, i.e. the level of input they received from the service. High-contact patients were defined as those attending the centre for two days per week or more, medium-contact patients as those attending, or seen by staff at home, at least once per fortnight. The data from both the 1984 and the 1987 census revealed a very different level of service input for men and women. Figure 1 shows that men constituted 72% of the 'high-contact' population in 1984 and 67% in 1987 while women constituted 28% of this population in 1984 and 33% in 1987. In both 1984 and 1987 there were approximately equal proportions of men and women in the medium- and low-contact groups. To state this another way, only 30% of women in 1984 and 29% of women in 1987 were receiving a high level of input from the service, as compared with 55% of men in 1984 and 45% in 1987. Thus in both 1984 and 1987 a higher proportion of men were receiving a high level of input from the service.

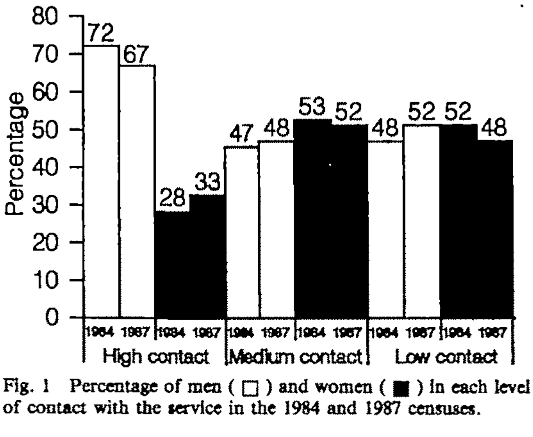

Fig. 1 Percentage of men (□) and women (■) in each level of contact with the service in the 1984 and 1987 censuses.

Discharge and movement within the service

In order to examine movement within and out of the service, patients level of contact with the service in 1984 and 1987 was compared (in terms of high, medium or low contact or no longer within the service). The proportion leaving the service was slightly higher for men than for women: 21.25% of men and 18.94% of women ceased contact with the service between 1984 and 1987. A total of 53% of men and 58% of women who were in high contact with the service in 1984 were still in high contact in 1987. Of the remainder of the 1984 'high-contact' patients, 7% of men and 6% of women were in medium contact, 16% of men and 12% of women were in low contact, and 24% of both men and women were no longer in contact with the service. Thus the pattern of changes in level of service input received by those who had received a high level of input in 1984 was very similar for men and women. Likewise, changes in level of service input for men and women who had been in low contact with the service in 1984 were similar. A total of 59% of men and 68% of women who had been in low contact with the service in 1984 remained at this level of input in 1987. Of the remainder of the 1984 low-contact group, in 1987 16% of men and 9% of women were in high contact with the service, 10% of men and 7% of women were in medium contact, and 16% of both men and women were no longer in contact with the service. This suggests a slightly, but not markedly greater degree of change in level of service contact for men than women in this 1984 low contact group.

The picture was quite different for the 1984 'medium-contact' patients. A total of 17% of men and 39% of women who had been in medium contact with the service in 1984 remained in medium contact with the service in 1987. Of the 1984 male medium-contact patients, 28% were in high contact with the service, 27% were in low contact, and 28% had been discharged by 1987. Of 1984 female medium-contact patients, 10% were in high contact with the service in 1987, 32% were in low contact, and 19% had been discharged. These figures indicate that there was considerably less movement within and out of the service for women in the medium-contact category. Unlike their male counterparts, the majority of women remained in medium/low contact with the service over the three years. Given that there is no reason to assume that the functioning level and service input needs of men are likely to change more than those of women, this may suggest that the service was less responsive to the changing needs of these women.

Study 2: a survey of patients in high contact with the service

In order to examine sex differences in service provision a more detailed survey of patients in high contact with the service was conducted in 1986. In this study, detailed information was collected on all patients who attended the service on two days per week or more in a given month. This survey included 131 patients of whom 40% were women and 60% were men. The data collected included functioning level assessed by direct care staff using the REHAB assessment schedule (Hall & Baker, 1983) and information concerning usage of work areas and classes within the centre.

Functioning level

The REHAB assessment is a multipurpose behaviour rating scale designed to assess people with a major psychiatric handicap. A member of the direct care staff observes the patient for one week and then rates their behaviour on scales in two spheres: 'deviant behaviour' (incontinence, violence, inappropriate sexual behaviour, etc.) and 'general behaviour' (social activity, speech disturbance, self-care, and community skills).

In terms of 'general behaviour' scales, scores can be divided into three bands reflecting different levels of disability: 'severe handicap', 'moderate handicap' and 'mild handicap'. People scoring within the 'mild handicap' range are considered to have potential for community living with little support, while those scoring in the 'moderate' or 'severe' brackets are unlikely to be suitable for discharge and would require high levels of support if they were to live outside hospital (Hall & Baker, 1983). The distribution of general behaviour scores for men and women was very similar: 17% of men and 15% of women scored in the severely handicapped range; 30% of men and 33% of women scored in the moderately handicapped range; and 53% of men and 52% of women scored in the mildly handicapped range.

REHAB 'deviant behaviour' scores were divided into four bands related to the number of deviant behaviours in the observation week: 0, 1–2, 3–4 and ≥5. Once again, there were no marked differences in the amount of deviant behaviour exhibited by men and women (Fig. 2). A slightly higher proportion of men showed no deviant behaviour but exactly the same proportions showed high levels of deviant behaviour (≥5 deviant behaviours in the observation week).

Thus this data suggests that, in terms of functioning level, male and female patients in high contact with the service were very similar. However, this similarity was not reflected in their use of workshops and classes within the centre.

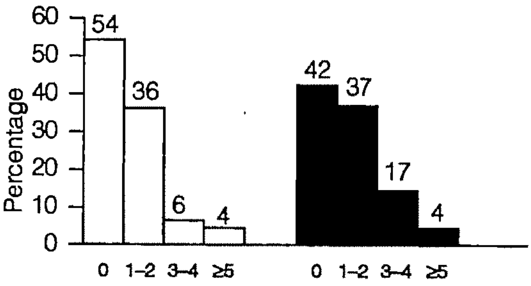

Fig. 2 Percentage of men (□) and women (■) with scores on the REHAB deviant behaviour scale of 0, 1–2, 3–4 and ≥5 (0 indicates a low level of deviance and ≥5 a high level).

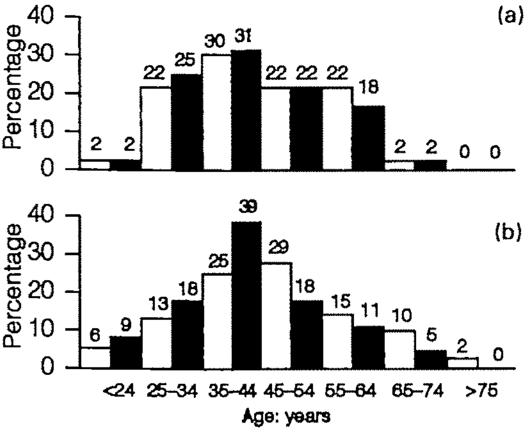

Fig. 3 Age distribution of (a) men and (b) women in the 'high-contact population' (□) and in workshops and classes (■).

Use of workshops and classes

Of the 131 'high contact' patients, 82 (63%) were involved in workshops or classes: 57% went to workshops and 24% to classes (self-care, cookery, literacy, art, gardening, etc.). Overall, the ratio of men to women in workshops was an almost exact reflection of the population as a whole: women comprised 40% of the population of high-contact patients and 37% of workshop users. In the classes the position was reversed: 58% of class users were women. Thus proportionate to their numbers in the population, women made greater use of recreational and skills training classes than men.

Taking age into account as well, Fig. 3(a) shows that the distribution of ages of men in workshops and classes was similar to that in the population as a whole. On the other hand, Fig. 3(b) shows that organised activities such as workshops and classes predominantly served younger women (≤45 years); 56% of women were aged over 45 years, yet only 34% of women using workshops and classes were in this age bracket. Thus it appears that the organised activities at the centre were not providing a service for older women, many of whom spent their time doing very little.

The industrial workshops at the centre were theoretically organised on the basis of functioning level on a 'throughput' model. Workshop 3 was designed to cater for those functioning at the lowest level, workshop 1 and the clerical workshop were seen as places where people could be prepared to move on either to sheltered employment outside the hospital or to open employment. In theory, people were promoted through the workshops from 3 to 2 to 1/clerical, until their optimal level of functioning was reached and further progress was unlikely.

However, there were marked differences in the services provided for men and women by these various levels of work facility. Figure 4 shows that men were

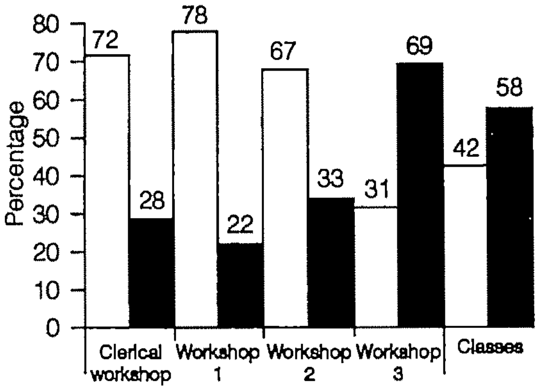

Fig. 4 Proportion of men (□) and women (■) in different workshops and classes (where the clerical workshop is for those with higher functioning level and workshop 3 for those with lower functioning level).

over-represented in the work areas designed for those functioning at a higher level, while women were over-represented in the lower functioning level ones. Women comprised 22% of the population of workshop 1 and 69% of the population of workshop 3. This pattern cannot be accounted for in terms of differences in the functioning level of men and women as the distribution of functioning level of male and female attenders was very similar (in terms of the REHAB scores).

Discussion

The picture that emerges from the above data suggests that chronically mentally ill women received a markedly different input from the rehabilitation and continuing care services than their male counterparts. The women appeared to have been in contact with the services for longer, to have received less intensive input from the services, and it is possible that the services had been less responsive to their changing needs, especially for those in medium contact with the service (less than twice per week but more than once per fortnight).

As compared with their male counterparts, women in the 'medium-contact' group were less likely to have been discharged between 1984 and 1987, and were less likely to be receiving a higher level of input in 1987 than they were in 1984. That is, they were more likely than men to have been receiving the same level of service input in 1984 and 1987. If there were reason to assume that men and women differ in the extent to which their needs change over time then this might explain this pattern of findings. However, while changes in needs and service responses to these were not examined directly in this study, there are no grounds for assuming that men's needs change more than women's. Therefore it seems reasonable to hypothesise that services were more responsive to the changing needs of men than women. Clearly, further enquiry is necessary in this area, and the reasons for this possible lack of service responsivity to changing needs cannot be ascertained from the present data. However, it is possible that women in this 'medium-contact' category were relatively less demanding than their male counterparts and it was therefore easier for services to overlook their needs for changes in level of input provided.

If it were assumed that functioning levels of male and female service users differed, with women functioning at a higher level than men, then this may explain the differences in service input received. Data on functioning level of medium-contact patients was not collected in this study, therefore this possibility cannot be examined directly. Although no differences were found between the functioning of men and women in the high-contact category, this does not indicate an absence of more disabled women in the medium-contact category who could have benefited from higher levels of input. Once again, if disabled women were relatively less demanding of service input than men this might explain their under-representation among those receiving a high level of service input.

Within the group of patients in relatively high contact with the service (two days per week or more), the functioning level of men and women did not differ. However, once again, the service that they received did. Women were over-represented in recreational and skills training classes, and over-represented in work areas designed for those functioning at a lower level, despite an absence of evidence of lower levels of functioning as compared with men. Taking age into account as well, women over the age of 45 years appeared to be particularly badly served by the organised activities at the centre – many spent large proportions of their time doing very little.

It might be argued that this pattern merely reflects the typical employment patterns of women and lower levels of achievement found in non-psychiatric female populations. However this cannot be taken to constitute a reason for the over-representation of women in work areas designed for those functioning at a lower level. Firstly, all the work offered at the centre is of a type typically performed by women in non-psychiatric populations (packing, light assembly work, clerical work, etc.). Secondly, and more importantly, the underachievement of women in non-psychiatric populations does not constitute a justification for the patterns found in the sheltered environment of the centre. The work offered did not constitute employment retraining, rather it was constructed as a therapeutic activity. That women were found in the areas designed for the less able, and that older women were getting less of it, is a point of major concern. That work is therapeutic and inactivity deleterious to the functioning of severely disabled long-term patients has been amply demonstrated (e.g. Wing & Brown, 1970; Bennett, 1970; Shepherd, 1984). Thus women ought to be getting an equal amount of a level commensurate with their needs.

The data presented here clearly suggest that the rehabilitation and continuing care service considered provided a markedly different input for its male and female users. The nature of these differences raises questions about whether the needs of female patients were being adequately met. Clearly such questions, and the reasons for the differences found, require further investigation. For example, it is possible that the women users themselves perceived the services as less relevant and therefore used them less. Alternatively, it may have been the lower levels of expectation of others (staff, family, etc.) that resulted in the lower levels of service input provided to men and women.

Similar explanations may be offered for the different patterns of usage of organised activities by those in high contact with the service. The higher level work activities may have been viewed as a largely 'male' preserve. It is possible that by offering activities more relevant to the needs of women, particularly older women, usage would be increased. Alternatively, the activities themselves may in principle have been appropriate, and differences in usage a result of differing expectations.

Whatever the explanation for the present findings, the data presented here clearly indicate that more attention must be paid to issues of gender in rehabilitation and community care. It cannot be assumed that the same service will be equally appropriate for men and women and more detailed investigation of the service needs of chronically mentally-ill women is required.

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Where do People with Long-Term Mental Health Problems Live?
A Comparison of the Sexes

ALISON M. CONNING and L. A. ROWLAND

The closure of large psychiatric institutions has led to alternative accommodation being developed for people with long-term psychiatric disabilities, with an emphasis on group living. Despite this, very little is known about where these people live, about the accommodation needs of this group, or whether men and women have differing needs. This paper examines the accommodation of all people with long-term and severe psychiatric disabilities in one South London borough who were in contact with a specialist service. It was found that the majority of people either live with their families – although the family member differed for men and women – or live alone. Men were more likely than women to live in hostels or alone, while women were more likely than men to live with their families.

The recent movements towards deinstitutionalisation, and care in the community, have led to many Health Authorities developing new service provision for people with long-term and severe mental health problems. As this client group previously lived in long-stay hospitals, much energy has gone into planning alternative forms of accommodation.

Some Health Authorities have tried to provide a range of housing (Lovett, 1984; Reed, 1984; Garety, 1988) but the emphasis has been on group living (e.g. Apte, 1968; Weinman & Kleiner, 1978; Wykes, 1983; Gibbons, 1986; Rowland, 1986; Thapa & Rowland, 1986; Wing & Furlong, 1986; Felce *et al*, 1985; Bates & Walsh, 1989), particularly staffed hostels and group homes (Garety, 1988). It is argued that group living is preferable because it prevents loneliness. Although there have been descriptive reports of hostels and group homes (e.g. Ryan & Hewitt, 1976; Ryan & Wing, 1979; Pritlove, 1983), and evaluations of individual projects (e.g. Wykes, 1983; Garety & Morris, 1984; Goldberg *et al*, 1985; Gibbons & Butler, 1987), policy makers do not have sound knowledge upon which to plan optimal living arrangements for people with long-term psychiatric disabilities (Hill, 1988).

Recently a few studies have looked at residents' attitudes towards their group living arrangements. These studies have found that residents do not consider themselves to have close friendships with other residents (Pritlove, 1983; Hill, 1988), although they may go out together sometimes, and help each other with personal and practical problems (Pritlove, 1983). Staff have a rosier picture of the extent of friendly interaction between residents than do the residents themselves (Pritlove, 1983). For some individuals the socially stimulating environment created by group living produces florid psychotic symptoms (Falloon & Marshall, 1983). Many people who live in hostels or group homes are dissatisfied with their accommodation (Lehman *et al*, 1982; Hill, 1988; Kay & Legg, 1986; Waismann, 1988), and would prefer to live alone (Lehman *et al*, 1982; Kay & Legg, 1988), although they recognise that their choice is limited (Hill, 1988).

It is often assumed that people who are placed in hostels are more disabled than those who live alone. However, Waismann (1988), using the REHAB rating scale (Hall & Baker, 1983), showed that a large proportion of people living alone are severely disabled (Table 1). Hostels/group homes can only accommodate people who can cope with group living, and are often intolerant of difficult behaviour (Hill, 1988).

Table 1
A comparison of levels of functioning across types of living arrangements (from Waismann, 1988)

General behaviour scale (REHAB)[1]	Resident at DSC[2]	Alone	Hostel	Family
Mean score	57.7	39.0	35.1	29.8
% scoring 0–41 ('discharge potential range')	4.9	23.9	12.9	58.3
% scoring 41–65 ('moderate handicap range')	10.1	30.2	19.6	40.2
% scoring >65 ('severe handicap range')	30.0	36.0	6.3	28.6

1. The REHAB rates 'general behaviour' and 'deviant behaviour'
2. District services centre

It has been claimed that many Health Authorities have failed to provide alternative accommodation for people who used to live in long-term psychiatric institutions (Patrick *et al*, 1989; Garety, 1988). As a result, large numbers of people with mental health problems are homeless (Priest, 1970, 1971; Lodge Patch, 1971; House of Commons Social Services Committee, 1983; Marshall, 1989). This is a serious problem not least because it is difficult to deliver psychiatric services to people who are homeless (Abdul-Hamid & McCarthy, 1989; Bachrach, 1984).

The homeless population has traditionally been made up of men, but the number of homeless women is growing (Scott *et al*, 1966; Priest, 1971; Weller *et al*, 1987). This is probably due, at least in part, to the closure of psychiatric institutions. Yet most of the accommodation available to the homeless is only for men (Weller *et al*, 1987).

Recent studies have looked at what contributes to the quality of life of people with long-term psychiatric disabilities. Both Waismann (1988), studying 83 people in contact with psychiatric services, and Thapa & Rowland (1989) who studied 31 chronic psychiatric patients, found that the nature of people's accommodation was one of the most important contributors to quality of life. People with long-term mental health problems rated living conditions as a more important contributor to quality of life than did those without such problems (Thapa & Rowland, 1989). These findings make it even more important that bodies planning accommodation for this client group get it right.

Given the importance of satisfactory accommodation for people with long-term mental health problems, the high proportion of such people among the homeless, and the insufficient data on appropriate accommodation for these people, several questions need to be answered. Firstly, where do people with long-term mental health problems live? Secondly, what sort of accommodation best serves their needs? And thirdly, do men and women have different accommodation needs?

This paper begins to address the first of these questions by examining the accommodation of people with long-term mental health problems cared for by one service. This service has been established for nine years and so has had time to develop and use a range of accommodation without the pressure of imminent hospital closure. The second and third questions are discussed with reference to these data.

Method

The patients surveyed were all people with long-term and severe psychiatric disabilities, served by the District Services Centre (DSC), Maudsley Hospital, Camberwell, London (see Perkins & Rowland, 1991). The DSC provides the service for people from the client group living in South Southwark, who can be day patients who attend every day, part-time day patients who attend approximately three days a week, supportive patients who attend between once a week and once a month, and domiciliary patients who do not come to the DSC but are visited at home. The DSC has 34 beds for short-term admissions for people who are in a crisis, and for those for whom suitable alternative accommodation has not yet been found.

In 1984, 1985 and 1987 on 28th August, one-day censuses were carried out on all of the patients served by the DSC. The data collected included the name of the patient, date of birth, sex, date of admission to DSC, present status (resident, day patient, etc.), and accommodation (resident at DSC, hostel, family, alone, other). In 1990, data was gathered on each patient's living situation using the same accommodation categories as in the censuses, but breaking the 'family' category down into four smaller categories: lives with spouse/partner, lives with parent, lives with child and lives with sibling.

In addition the local hostels were examined in terms of the number of places available and the sex of the residents to whom they offer places.

The DSC runs an Accommodation Bureau, which compiles a list of patients awaiting hostel places and their level of disability, plus the number and type of places available in each hostel. The referrals to the Accommodation Bureau over the six months since it began were examined.

Table 2
Accommodation of DSC patients

	Resident at DSC	Hostel	Family	Alone	Other	Total
1984 census: n (%)	19 (8%)	48 (20%)	121 (50%)	53 (22%)	0	241
1985 census: n (%)	17 (8%)	33 (15%)	107 (49%)	61 (28%)	0	218
1987 census: n (%)	9 (4%)	31 (14%)	95 (43%)	76 (34%)	11 (5%)	222
1990 census: n (%)	19 (7%)	50 (18%)	109 (40%)	89 (33%)	7 (3%)	274
Mean %	6.8%	16.8%	45.5%	29.3%	2%	

Table 3
Accommodation of men and women in the DSC in 1987 and 1990

	Resident at DSC	Hostel	Family	Alone	Other	Total
1987 census						
Men: n (%)	11 (8%)	20 (15%)	52 (40%)	47 (36%)	1 (1%)	131
Women: n (%)	5 (6%)	11 (12%)	43 (47%)	28 (31%)	4 (4%)	91
1990 census						
Men: n (%)	13 (7.9%)	32 (19.5%)	61 (37.2%)	55 (33.5%)	3 (1.8%)	164
Women: n (%)	6 (5.5%)	18 (16.4%)	48 (43.6%)	34 (30.9%)	4 (3.6%)	110
All men = mean %	8%	17.3%	38.6%	34.8%	1.4%	
All women = mean %	5.8%	14.2%	45.3%	30.6%	3.8%	

Results

Table 2 shows the distribution of patients across the five accommodation categories used in the censuses of 1984 (Perkins & Rowland, 1984), 1985 (Rowland, 1985), 1987 (Rowland, 1987) and 1990. The majority of people live with their families (45.5%). More people live alone (29.3%) than in hostels (16.8%). Over the last six years there has been a trend towards a smaller proportion of people living with their families (by 10%), although this is still the largest category.

For 1987 and 1990 this data was broken down by sex (Table 3). Women comprised about 40% of the DSC population. A greater proportion of women than men lived with their families (45% : 39%), a greater proportion of men than women lived alone (35% : 30%) or in hostels (17% : 14%).

Hostel accommodation

The Accommodation Bureau services 14 hostels/group homes run by six charitable organisations. They offer a total of 119 residential places, with varying amounts of staff support. Not all of the hostel places are taken by DSC patients. Some of the hostel residents come from outside the Borough, but become DSC patients after their move to the district. Sixty-one (51.3%) of the places are available to men only, 12 (10.1%) to women only, and 46 (38.7%) to people of either sex. Six of the hostels/group homes are open only for men, and one for women only.

From August 1989 to January 1990, 48.3% of the hostel places which became available were for men, 20.7% were for women, and 31% were for either sex. Over this six months, 66.1% of the monthly referrals to the Accommodation Bureau were men, and 33.9% were women. Of those who were removed from the waiting list, presumably because accommodation was found, or hostel accommodation was no longer thought to be suitable, 38.9% were women, and 61.1% were men.

Family accommodation

Table 4 shows the number and percentage of each sex who lived in each type of accommodation in 1990. A total of 43.6% of women and 37.2% of men lived with their families. Of these, more women lived with their spouse/partners (28.2% : 8.5%), or with their children (8.2% : 1.2%), while more men lived with their parent(s) (25.0% : 6.4%).

Discussion

Despite the emphasis on providing group living arrangements for people with long-term psychiatric disabilities, only 17% of long-term psychiatric patients in South Southwark live in hostels, while 46% live with their families, and a substantial minority live alone (29%). Others have found a much smaller proportion of people living with their families (Bates & Walsh, 1989) than in the present study. This difference may be because the DSC has been operating for nine years and so some clients have not been isolated from their families in psychiatric institutions, but have continued living at home.

Over the last six years there has been a decrease in the proportion of people living with their families, and an increase in the proportion of people living alone.

Table 4
Number and % of men (*n* = 164) and women (*n* = 110) who lived in each type of accommodation (1990)

	Resident at DSC	Hostel	With spouse/ partner	With parent	With child	With sibling	Alone	Other
men: *n* (%)	13 (7.9%)	32 (19.5%)	14 (8.5%)	41 (25%)	2 (1.2%)	4 (2.4%)	55 (33.5%)	3 (1.8%)
women: *n* (%)	6 (5.5%)	18 (16.4%)	31 (28.2%)	7 (6.4%)	9 (8.2%)	1 (0.9%)	34 (30.9%)	4 (3.6%)
Total: *n* (%)	19 (6.9%)	50 (18.2%)	45 (16.4%)	48 (17.5%)	11 (4.0%)	5 (1.8%)	89 (32.5%)	7 (2.6%)

While there are no data on the cause of these changes, for the older clients it may be due to the death of a spouse/partner, or sibling. Other possible reasons are the breakdown of a relationship, grown-up children leaving the client's home, or the client moving out of his or her parents' home.

The distribution of patients across accommodation types was different for men and women. A higher proportion of women than men lived with their families, a slightly higher proportion of men than women lived alone, and a slightly higher proportion of men than women lived in hostels.

The sex difference in hostel living could reflect the proportion of hostel places available to each sex: 90% of group living places could accommodate men, and only 49% could accommodate women. However, this does not seem to be the answer. Women were judged by staff to be less in need of such accommodation than men as only 34% of the referrals to hostels were for women. The higher proportion of men than women in hostels/group homes is a common finding (Garety & Morris, 1984; Gibbons, 1986), and may reflect a real difference in need between the sexes. One possible explanation is that men who do not have a partner, and who have previously been cared for by parents, tend to move into, or are placed in, accommodation where they are still cared for, this time by hostel staff.

Of those who live with their families, women are most likely to live with their spouse/partner or child, and men are most likely to live with their parents. This may reflect the fact that the marriage rate for female schizophrenics is higher than for male schizophrenics, and that the marriages of female schizophrenics tend to last longer than those of male schizophrenics (Erlenmeyer-Kimling *et al*, 1980).

About a third of the men and women studied here lived alone. As relationships are one of the most important contributors to quality of life for people with long-term psychiatric problems (Thapa & Rowland, 1989; Waismann, 1988), ensuring the opportunity to be with other people is an important area of service provision for patients who live alone. It is important to ensure that a range of social contact is possible, as people have differing needs. For example, other patients are often part of a coherent network of acquaintances and friends for female patients. For many male patients just being in the company of others is valued (Mitchell & Birley, 1982).

Women with long-term psychiatric problems appear to be better than men at forming relationships which lead to marriage or cohabitation, sustaining those relationships, staying in close contact with their families, and forming networks of friends. This is reflected in the types of accommodation in which they live, and the over-representation of men in group-living accommodation.

Placing a patient in a flat alone is often the best option, particularly if he or she has antisocial habits (e.g. playing loud music in the early hours of the morning) or finds it difficult to be with others for long periods. People can manage to live alone despite severe psychiatric disabilities (Waismann, 1988), although survival alone may only be possible with extensive support and practical help, such as with cleaning, meals, and paying the rent and electricity bills. In particular, staff may need to find ingenious ways of equipping a patient's flat adequately. It costs £1022 for basic furniture using furnishings which meet the safety standards of the Trading Standards Office, and the DHSS Regulations of 1980–86 (Bates & Walsh, 1989). If the individual is 'lucky' enough to receive a start-up grant of £500, this will not stretch far.

Conclusions

This paper shows that a large number of people with long-term psychiatric disabilities can survive in accommodation alone, or sustain family relationships (with a parent, spouse/partner, child, or sibling) to an extent that they can live with their relatives. This has several implications for the services provided for these individuals. For those living alone, practical help and appropriate social contact may be of paramount importance. For those living with their families, contact with the family by the service providers, help for the family where needed, and time away from the family, are likely to be of primary importance.

In the population studied here there were sex differences in where people lived. Women were more likely than men to live with their families, and for those families to be spouses/partners or children, rather than parents. Men were more likely than women to live in hostels or group homes. This probably reflects the differences between the sexes in their abilities to make and sustain close relationships, and the differing roles which men and women traditionally play within the family.

When deciding on the type of accommodation in which an individual with long-term psychiatric disabilities should live, a number of factors should be taken into account: his or her own preference, his or her ability to make and sustain social relationships and to tolerate social interaction, the extent and nature of his or her antisocial behaviour (if any), and the availability of practical help.

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Psychology and Psychopathology in Women – A Psychoanalytic Perspective

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Aspects of the normal psychology and psychopathology of women are discussed in relation to adolescence, young womanhood and motherhood. Perversions of motherhood exist, although they are largely denied by a society which idealises being a mother. This denial may be caused by society's inability to see a woman as a complete human being. The aetiology of perversions in women is both psychobiological and social and it is bound up with the politics of power. Perverse motherhood can be seen as the product of the emotional instability and inadequate individuation brought about by a process involving at least three generations.

Whereas psychology studies what has been called normal psychic life, psychopathology is concerned with the ill person as a whole, in so far as she suffers from a psychic illness.

The problem though, is that normality is extremely difficult to define, so its definition is generally deduced from the absence of marked psychopathological traits. I have found case study to be the most suitable technique for the study of psychopathology. Discovery often consists of simply listening to the patient attentively, with an open-mindedness and readiness to record facts previously ignored because they were too uncomfortable or painful to hear. A patient talking about her case history can throw light on 'new', different or previously ignored or unrecorded female psychic phenomena.

In this article I use the uncustomary female pronoun in an attempt to make us both, women and men, aware that we women – one half of the human race – are different from the other half. If we always use the male pronoun to mean both male and female we get into the habit of supposing that what is true for the male, is equally true for the female. We women are ready now to explore our own female identity and to accept our own systems and predicaments. It is about time that we shared our growing insight with the other half. And who knows? Perhaps in the near future we could be understood without biases, false assumptions, half compromises and even deceit. It is not surprising, given the lack of understanding which exists, that many women presenting to doctors with psychological problems are treated with tranquillisers, effectively blocking fuller exploration of the problem and diagnosis of other female psychopathology.

For a long time we women have been silent conspirators in a system where the male is the master and the female the consenting counterpart. It is possible that this is how our ignorance about women's psychology and psychopathology began, especially in relation to sexuality. Not only was the assumption made (false, of course) that all normal female psychology was the counterpart or the parallel to men's normal libidinal development, but it was also assumed that the psychopathological findings had to be identical in both genders. Hence, whatever was considered to be abnormal for men was expected to appear also in women. We were 'understood' in our psychological growth as little boys without penises – not too subtle; especially considering the richness of our own reproductive organs. Since men had resorted to perversion as a way to deal with the fear of losing their penis, women were left in a position in which perversions were not available to them. We could then say 'Women can't have perversions because they can have babies'. Furthermore, according to the same old theories our 'penis envy' problems were only resolved with the wish to have Daddy's baby. Pregnancy and motherhood were then considered to be the resolution of our phallic desires. The symbolic equivalence between penis and baby was created.

Without any questioning, motherhood was considered a healthy psychological expression of emotional maturity and a manifestation of mental stability. The only exception to this rule, single motherhood, was due entirely to moral attitudes. No wonder we women have been left with some important problems not only unresolved but also undiagnosed. In fact, severe female psychopathology has been left unrecorded and ignored because it would have challenged stereotyped, traditional views glorifying motherhood and completely denying its negative possibilities.

In the 1960s we failed to acknowledge what really happened with 'battered babies'; nobody, even experienced physicians, could believe that those babies' injuries had been caused by their mothers. Two including maternal incest. And why? Because otherwise we should have to accept a complete different psychopathology from what is usually believed, one which originates from the female body and its inherent attributes, and which involves the woman using her reproductive organs for the expression of perversions.

I use the term perversion rather than deviation since the latter implies only a statistical abnormality. In my own terms perversion is a clinical condition in which the person afflicted does not feel free to obtain sexual genital gratification but instead feels 'taken over' by a compulsive activity. Achievement of intimacy with a partner through sexual intercourse – the norm – is replaced in perversion by release from increasing sexual anxiety through a bizarre action or situation which is in itself inexplicable not only to others but also to the person herself (Welldon, 1989). Why is it so difficult to conceptualise the notion of perverse motherhood when there is evidence that male perversion is often the result of early faulty mothering?

I follow the object-relations theory put forward by Melanie Klein and others, particularly Fairbairn, Winnicott and Balint and in general the so-called Independent Psychoanalysts (Kohon, 1986). This stresses the importance of the first few months of life and the infant–mother relationship. I am using the word 'object' as opposed to subject, and 'part-object' when the person finds it impossible to see the other person or 'object' as a whole and separate being. Object relationship is only achieved in emotional maturity, in the post-oedipal stages. The pre-oedipal phase is currently thought to account for future perverse psychopathology, in which the psychogenesis is deeply related to intense fears of being either abandoned or seduced by mother.

Klein's theories centre on the infant girl's intense envy of her mother's reproductive functions (Klein, 1932). This creates in her great hostility towards her mother which develops into frustrated fantasies of entering into and robbing mother's body of its entire contents. Using projective identification, she assumes that her mother will rob her of her own procreative capacities. I have observed the occurrence of those mental mechanisms in the women I treat and believe they become the equivalent of castration fears in the boy.

As a clinician, I have observed that the main difference between a male and a female perverse action lies in the aim. Whereas in men the act is aimed at an outside part-object, in women it is against themselves, either against their bodies or against objects of their own creation, that is, their babies. In short, bodies and babies are treated as part-objects (Welldon, 1988).

The reproductive functions and organs are used by both sexes to express perversion. Perverse men use their penises to attack and show hatred towards symbolic sources of humiliation, usually represented by part-objects. If perversion in the man is focused through his penis, in the woman it will similarly be expressed through her reproductive organs and the mental representations of motherhood.

Normal psychology and psychopathology are different phenomena at different junctures of a woman's life. They might partly depend on the circumstances surrounding her own birth, and later on precipitating factors related to attitudes regarding her own gender, which will reappear at times of change intimately associated with the female body. To be more specific, look at particular psychopathologies which appear at different times, associated with adolescence, young womanhood and motherhood. Throughout this enterprise it is an inescapable fact that we are already mixing up femininity with motherhood and woman's capacity for procreation. Such is the confusion of the terms: femininity, womanhood, female sexuality, motherhood – all are used at different times to impart the same meaning. Even my womens' groups composed of highly sophisticated professional women, when faced with a questionnaire regarding those terms are at a loss to define them.

From the moment of conception, all sorts of fantasies populate the pregnant woman's mind and will be responsible for the new being's future development, which in turn will largely depend on the welcoming or unwelcoming attitudes towards its gender. This will be especially crucial for generations to come if a girl is born when a boy was expected, since not only that woman's future emotional development is at stake but also that of her own children. The woman's capacity for procreation not only affects her emotional life but also her mental representations of her body. In a way, one could predict that the less expectations the future mother has about her new baby's gender, the more relaxed she feels about it. On the other hand she may respond to other family members or to her own internal pressures to produce a specific type of baby. This is a neat example of how difficult it is for a woman to have access to her own wants and expectations.

Psychology

Some features of female psychological development

We need to understand at least two different but inter-related phenomena in order to make hypotheses about female sexual psychology and its psychopathology.

One phenomenon concerns 'inner space', a term coined by Erickson (1968), equated not only with pregnancy and childbirth but also with lactation and all parts of the female anatomy which stands for fullness, warmth and generosity. The second phenomenon concerns time, which is related to rhythmicity and biology. This is 'the biological clock'. It is particularly important in adult decisions about motherhood, especially when 'time is running out'.

The 'inner space' and the 'biological clock' are different phenomena but their effects intertwine. In the maturational crises in women's lives sometimes one is more important, sometimes the other. In adolescence the 'inner space' tends to be the more important of the two in relation to fantasies about pregnancy, while later the 'biological clock' can be more insistent. At menopause the two come together.

Whereas a man owns the 'freehold' of his reproductive organs, a woman has only a 'leasehold'. In pregnancy 'the owner-occupier' is not only taking over her body, but also her mental representations. So when does the woman feel her body and its mental representations to be completely her own?

The first menstrual period – the menarche – heralds the girl-woman's fecundity. Then she will have periods every four weeks – the menses – which are a constant reminder of her hope-dread of it. They will remain for years to come, yet those years are limited. Adolescence gives a second chance for reassurance of the gender identity. This is if all circumstances are propitious to the girl developing into a young woman, who will be able to enjoy a growing sense of femininity and later of womanhood.

As I have indicated, there is an important generational aspect to female psychology and psychopathology – grandmother, mother, daughter and so on. Therefore in principle every stage in life can be important to the problem as a whole. But my present purpose is explicitly to discuss female perversion in relation to motherhood. In such a context the menopause seems not totally relevant, yet it would be foolish to deny that there could be a psychopathology connected with the menopause. This is a subject which I hope to address on a future occasion.

Female libidinal development

For women the act of making love takes on a unique dimension since they are aware of using the same organ for sexual pleasure as for procreation. They know from the very primitive roots of their identity as women that they have a reproductive organ, which in the event of sexual intercourse might produce a pregnancy that will change their bodies drastically, if temporarily, and will also deeply affect their whole lives. Before the contraceptive pill women felt at times torn between their emotional-instinctive drives towards wanting to make love and intense fears of the consequences, such as an unwanted pregnancy. Only with the arrival of AIDS have I heard similar comments made by men concerning the consequences of casual sex, such as: "I can't believe it, *only once* and one could get it".

Several women, not only my patients, have told me of their certainty during coitus of the most blissful kind that they had just conceived; and the timing of birth has borne out their feelings. This seems to be a deep feminine instinct, for even barren women have told me of their conviction that had they been able to conceive they would have done so at the climax of a perfect sexual union. Such is – or can be – women's awareness of their bodies and their mental representations.

Pregnancy

Pregnancy concentrates the mind on reality. It has often been said that female sexuality remains 'a riddle' (Freud, 1931) and that this might have to do with women's sexual organs being 'hidden away', making the subject obscure. Certainly this argument loses part of its power when related to the changes in the female reproductive organs during pregnancy. These changes are so manifest that they give rise to powerful feelings in both men and women. Breasts and uterus swell and change. The breast is not only linked to nurturing functions but also is a focus of sexual stimulus, in other words, capable of producing sexual pleasure without necessarily any direct link to a vital function. In some women any sexual pleasure related to their breasts ceases not only in pregnancy but for years after weaning has occurred. Such women experience a tremendous sense of loss when they renew love-making with their partners and become aware of this missing dimension. Some of them had breastfed their babies for up to two years; some had found this sexually gratifying but not always. They considered that perhaps with the arrival of the baby an important part of their bodies had been made redundant as a site of sexual stimulation and that perhaps their rights to this pleasure had been superseded by the new function, so much more vital in its deep relationship to the nurturing of their offspring.

Normal motherhood

Normal child development depends predominantly on healthy mothering, in which mothers obtain an important degree of pleasure from the process of taking care of their babies and helping them to develop into independent and self-assured human beings, with their own unique characteristics and their specific gender. Although through 'good enough mothering', babies achieve their 'true self' (Winnicott, 1965), this is more easily said than done, since mothers are also the children of their own mothers, with their own plethora of early experiences and traumas.

Women's fears about becoming mothers run, sometimes simultaneously, with a tremendous sense of power in procreativity. Their dreams and fantasies when ready for procreation may later materialise in the most intimate relationship with a baby of either sex: such is the degree of emotional intimacy and physical dependency that women can create in any new human being, regardless of sex. This early dependency on women can produce not only physical but also emotional marks. Women have the monopoly of providing or inflicting very early and decisive influences on their offspring, but this monopoly starts operating only when they have reached maturity in their reproductive functions. In preparation for this sense of power, girls usually have fantasies of procreation played out with their dolls, friends and siblings in which they behave like good mothers or nasty-ugly surrogate mothers.

Let us think just in female terms for a minute. Nesting in the female body is that male body which, according to traditional psychoanalytical views, arouses feelings of envy, competition and rivalry in women. Women in their maternal role experience a sense of bewilderment and intense excitement about having baby boys. After all, they are containing within themselves the wonders of the opposite sex. In some, a secret wish to produce a baby boy might be associated with feelings of accomplishment, because mother did not give birth to one.

A woman who has a baby girl sees a replica of herself, a woman, as she mothers her daughter. This produces in normal circumstances, a deep feeling of connectedness and loving security. We could also say that girls have a unique experience in having their first object-relationship to their own gender.

Psychopathology

Adolescence and promiscuity

Sometimes young women may feel awkward and insecure in dealing with their powerful feelings about the tremendous changes occurring inside and outside their bodies, especially if they are not supported by their mothers in their acknowledgement of their sense of femininity. After all, while some mothers of adolescent boys show off with them and obtain narcissistic gratification when mistakes are made about their relationship, the same mothers, when in the company of attractive adolescent daughters, feel put down and disregarded by the men who make complimentary remarks about their daughters. Young girls' bodies are openly on display with all their fresh beauty while mothers are ageing. A tremendous sense of competition may emerge, especially if mothers are approaching menopause. The adolescent boy has an easier transition from attachment to mother to another woman than does the adolescent girl, since the boy does not need to change his first love object. The girl, instead, has to make the switch from attachment to mother to attachment to father.

The way fathers respond to their daughters' difficulties regarding the latter's incipient sexuality is important. If a father is dismissive and inattentive, the adolescent will feel undermined and disparaged. If father is critical and denigrating, she will feel devastated. This could then be expressed by the typical adolescent rebelliousness which may include promiscuity, a compulsive and indiscriminate 'sexual' search, which actually has little to do with genital sexuality and is only experienced as a 'solution' to deal with rejection by first the mother and then the father. Promiscuity is then basically a compulsive illusory attempt to create object-relationships, which is doomed to failure since the young woman is really flying from a frustration with mother, who she feels to be unable to provide her with good nurturing. She is now in a compulsive and non-selective way looking in men for what she missed in her contact with her mother. So, more disappointments are on the way. They are rooted in two different sources: real mother and symbolic father-mother.

I have treated young girls who suffered from this type of problem and were receiving help at a therapeutic community. While there, they had many indiscriminate sexual encounters with rebellious young men. In so doing it was their secret wish to achieve a degree of intimacy which they had never experienced before. In this quest, a pregnancy could occur which left them with a sense of elation since they were now sure of belonging to the female gender. For some girls, the pregnancy itself was the ultimate achievement. In such cases, they would quickly seek an abortion. For others, the birth was necessary but only with the idea of giving the baby up as soon as it was born, in the belief that they could not take proper care of the new being. For others still, this pregnancy also offered help of a closeness with a growing foetus inside their bodies. At times, a sense of triumph in revenge against their mothers was present. They had now learnt that mothers' assumed hostile feelings towards them had not *really* damaged their capacities for procreation. This is why the mental representation of becoming a mother is at least a three-generational process. Woman becomes her mother and her mother's mother.

Prostitution as a sequel of paternal incest

My own clinical findings from patients who have been subjected to sexual abuse and incestuous behaviour often include a history of seduction and emotional deprivation, of being seen and treated as part-objects, of being prevented from individuating themselves from paternal figures and of being prematurely sexualised by their parents. These are similar characteristics to those found not only in the psychogenesis but also in the clinical manifestations of perversion.

Such women suffer from a depression which is disguised by compulsive genital sexual activity. Such activity is motivated by a deep need for revenge, and lacks intimacy, emotional nurturing, a sense of continuity and sexual gratification. Instead, it provides only short-lived elation which is soon replaced by a sense of isolation, despair and loneliness. Successful soliciting produces a manic response, 'a sense of high' which is very short-lived. (All these traits are almost identical to those found in male patients suffering from perversion.) This system of regulating the self-esteem is doomed to failure since the motivation is based on hatred as opposed to love and the objects encountered, whether represented by their own bodies or their clients', are mere symbolic replacements for the real ones against which they are directing their revenge.

Bulimia, anorexia and self-mutilation

The young woman may then resort in despair to other 'options', such as bulimia, anorexia nervosa, self-mutilation; all of them associated with irregularities of the menses, whose presence or absence could act as indicators of the severity of these syndromes. Such manifestations represent problems these young women have in accepting their own sexuality and its inherent biological functions. Such experiences are extreme cases of a conflictual situation with girls in adolescence. With the awakening of their inner sexuality and of their secondary sexual characteristics, a likening to their mothers' bodies appears. As a direct consequence, all unresolved early conflicts with mother become very alive, especially those related to frustration and anger.

Anxiety state due to the 'biological clock'

Some women who have shown determination at the beginning of their adult lives not to have children in order to advance professionally, come for therapy in their thirties, suffering from increasing anxiety and ambivalence about their long-held conviction of not wanting babies. Now they feel persecuted by time and by the approaching menopause. I have found that this is by no means a rare phenomenon, but it is far from inevitable. Many women when subjected to the pressures of the biological clock nevertheless achieve fulfilled womanhood whereas others are able to regain a sense of clarity in their true selves in pursuing exclusively their professions. Still others are able to combine both.

Female professionals and 'success anxiety'

Whereas men's intellectual achievements are usually viewed as consistent with their gender, women in parallel situations sometimes find themselves in conflict not only with the successful use of their intellects but also with their own femininity, which is often linked to the use of their bodies. At these times, women experience a split between their intellects and their femininity. This is especially so when a woman's mother has not used her intellectual capacities - sometimes due to socioeconomic pressures which her daughter does not share. Such a woman will fear success, believing that not only men but also her 'internal' mother will retaliate against her for her achievements. This can result in an extreme exaggeration arising from underrating of the intelligence while equating an overrating of the female body with femininity. Some professional women who come for therapy have considerable intellectual achievements with concomitant financial rewards. As opposed to men in equal positions who could easily have boasted about these successes, these women have difficulties in acknowledging them, and when they do it is with embarrassment and disbelief. It is as if they feel in open rebellion against traditional standards. In the course of their professional and social lives and despite themselves, they experience a mixed response when sexually approached by unattractive and uninteresting male colleagues. On the one hand, they feel humiliated and angry, but on the other, they feel secretly reassured and flattered by those unwanted approaches. Such is the bitter power that the female body and 'femininity' have been assigned as opposed to a woman's intellect.

Times are changing and so are women's expectations of themselves: they now experience more freedom and choice. However, for some women who have been subjected to their mothers' set of beliefs, in which they relied on their female bodies to give men sexual gratification and in their capacity for procreativity to secure a position of power in a man's world, there is a deep dread of challenging these old principles. These women are in constant fear of their mothers' envy about their own academic and intellectual achievements which they in their own times rarely had access to. This fear of success in women could become the equivalent of the fear of castration in men. The mother now becomes the 'internal saboteur' – internal mother – who is felt to repress other accomplishments.

Conflicts in motherhood regarding the future baby's gender

Problems arise however from the re-enactment of motherhood. The attitude the mother has towards the development of her little girl or boy is influenced by the way that she feels towards her own mother, the body mother provided her with and the way she felt accepted or rejected by mother as a child in her own gender. Thus, the birth of a girl might evoke in the mother the same response her birth created in her own mother. On the other hand, the birth of a boy can also create conflictual responses if this is felt to be a successful revenge against mother. I remember a patient in talking of the delivery of her son, saying: "When I heard that it was a baby boy I felt completely at peace. My mother, who has three daughters, looked at me and angrily said; how dare you, how dare you".

Another patient, whose baby was the first boy in three generations, first reacted with much pride and a sense of fulfilment which was soon replaced by an uneasy feeling. She told me how baffled she felt when she realised that she had begun to address him as a she and had a compulsive urge to buy for him very 'feminine' gear. This was her attempt to pacify fantasised envious attacks on her by her mother, grandmother and sisters. In other words, her sense of accomplishment had to be covered up by disguising the baby's gender in order to feel safe.

Perverted motherhood

There are very few psychoanalytical studies dealing with the particular psychopathology of perverse relations between mother and child. Whereas the mother's mental health emerges as crucial for the development of her offspring there is never an acknowledgement of the mother's perversion.

Whereas in psychoanalysis the word 'perversion' is used exclusively in relation to sexuality, before Freud's time the term was used to denote 'deviations of instinct' (Laplanche & Pontalis, 1973). It is interesting to note that there were descriptions of perversions of the 'moral sense' (delinquency), of the 'social instincts' (prostitution), and of the instinct of nutrition (bulimia, dipsomania). So it is strange that while the concept of instinct can be seen to stretch as far as nutrition and its abuse in dipsomania, no mention is made of the perversion of the 'maternal instinct' – a term which in the 'normal' sense has been so widely and loosely used. In other words, 'perverse motherhood' has never been acknowledged, with the rare exception by Rosen (1953). Rosen was concerned with the aetiology of schizophrenia and the understanding of the infant/adult who has suffered through the effects of the 'perverse mother'. In contrast, I am concerned with the behaviour of the mother herself.

Odd though it may sound, motherhood provides an excellent vehicle from which some women can exercise 'perversogenic' (Welldon, 1988) attitudes towards their offspring and also retaliate against their own mothers.

The importance of unconscious motivations to become a mother should not be overlooked. Raphael-Leff (1983) studied the models of mothering, as well as the effect (pact/impact) that the baby has on its mothers 'hopes and promises', in professional middle-class women. She describes two basic models of mothering. One is the 'regulator' in which basically the mother expects the baby to adapt to herself. The other is the 'facilitator' in which the mother adapts to the baby. It seems to me that in women with severe psychopathology, the facilitator mother, who welcomes the infant's dependence on her and their exclusive intimacy, is prone, when severely disturbed, to bring up transvestite, fetishistic and transsexual boys. On the other hand, the regulator mother could be more prone, again in extreme cases, to be the mother of battered babies.

A similar process has been described by Masterson & Rinsley (1975), who stress the mother's role in the aetiology of the borderline personality. The authors emphasise the effects on the baby of the alternation between maternal libidinal availability (reward) and its withdrawal at the time of separation/individuation. The baby, a future borderline personality, responds to mother's rewarding by the denial of separateness. This in itself confirms the child's acting out of its reunion fantasies with the maternal part-object, promotes its dependency, and reinforces its fears of being abandoned if it dares to individuate. Furthermore, Lothstein (1979) stresses the role of the mother in the aetiology of transsexualism in his studies on the mothers of male and female transsexuals.

Motherhood is sometimes chosen for unconscious perverse reasons. The woman knows that in achieving motherhood she is automatically achieving the role of master, that of being in complete control of another being who has to submit not only emotionally but also biologically to the mother's demands, however inappropriate they may be. Indeed, as is generally accepted, some women who feel inadequate and insecure find a child becomes the only available source of emotional nourishment and a craving for physical affection is unloaded on the child.

One of my patients was referred for a psychiatric assessment because of violent behaviour directed towards her second child. Although her first pregnancy came as a surprise to her, she still felt the need to go ahead with it, because in this way she felt she was taking out insurance against a dread of being alone. The child could become utterly dependent on her and totally under her control. When this first child arrived, she was overcome by feelings of repulsion against her baby. She felt ready to kick it, and after reflection she decided that in order to overcome these horrid feelings she would fix in her mind the idea of the baby being part of herself. Some days she would choose her right arm as being the baby, and at other times it would be one of her legs. In this way she felt able to master her impulses to beat up her first child. Later, with her second baby she asserted: "All the room in my body has been used up by the first one, there is no more room for a second one". It seems to me that one of the reasons we have stuck to the theory of the girl's penis-envy is in order to deny an unconscious awareness of mothers' unparalleled power over their infants in the early pre-oedipal phase.

Maternal incest

Do mothers commit incest more frequently than we think and more at the mother's initiative than we imagine? Are we blocked from perceiving this by our idealisation of motherhood? Surely this is why even in the original Oedipal situation we fail to notice the responsibility of Oedipus' mother, Jocasta. Hers is the most important case of incest. Everyone is ready to recognise paternal incest, but it seems much harder to believe that maternal incest could be happening – sometimes even to the mother's chagrin. So far as we know paternal incest is much more common, yet maternal incest exists and should not be wilfully ignored.

My clinical observations confirm this bias. On countless occasions, agencies and establishments have expressed alarm, sometimes verging on panic, when referring male patients to me as sexual abusers. This contrasts strongly with the difficulty my female patients have often had in being taken seriously by some agencies. Further, I have noticed that mothers are more ready to report incestuous feelings and actions towards their daughters than towards their sons. In the latter case, one does not hear until much later and then usually from the son's history.

We can observe that some of the psychodynamic principles operating in perversions appear in females when they become mothers. Woman's capacity for procreation – that is, getting pregnant and containing the baby within her own body – provides her with some of the same emotional characteristics in her object-relationships as are found in exaggerated and highly distorted forms in perverse relationships. These include the desire and intention to engulf the other person, to dehumanise the object, to intrude into, to invade, to be in complete control of and to merge with the other. My argument is that motherhood as a perversion occurs as a breakdown of inner mental structures, whereby the mother feels not only emotionally crippled in dealing with all those huge psychological and physical demands from her baby, but also impotent and unable to obtain gratification from other sources. She sees the world around her as non-existent in any supporting way. It is then that she falls back on inappropriate and perverse behaviour: that, in turn, makes her feel powerless. Simultaneously and paradoxically, she experiences her perverse behaviour as the only power available to her, through her exclusive emotional and physical authority over her baby. Hence perverse motherhood must be seen as the product of the emotional instability and inadequate individuation brought about by a process that involves at least three generations. But part of the problem lies with society in that our whole culture supports the idea that mothers have complete dominion over their babies. We encourage the ideas that the perverse mother then exploits. We do not help her or her children or society in general if we glorify motherhood so blindly as to exclude the fact that some mothers can act perversely.

Conclusions

The aetiology of perversion is intertwined with the politics of power. One aspect is the psychobiological and the other the social dimension. It is possible that the refusal to accept the existence of perversions in women is caused by society's inability to see woman as a complete human being. The difficulties in acknowledging that mothers can abuse their power could be the result of massive denial, as a way of dealing with this unpalatable truth. The woman is thereby seen as a part-object, or as just a receptacle of a man's perverse designs. The apparent idealisation of motherhood which is prevalent in society and blinds us to the existence of perverse attitudes ('women don't do those awful things'), thus contains a denigrating counterpart. Until recently a lack of legislation on female perversion – *pace* Queen Victoria – reflected society's total denial of it.

The study of power politics might throw new light on the understanding of motherhood functions. Perhaps if women had a longer tradition of belonging to the power structure their attitudes towards men and children would not be governed, as they are now, by a weakness which they strive to turn into possessiveness and control.

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LET WISDOM GUIDE

THE BRITISH JOURNAL OF PSYCHIATRY

June 1991 Vol. 158

Annotation

The marketing of 5-hydroxytryptamine: depression or anxiety? *D. Healy* 737

Review Article

Child psychiatry in developing countries. *A. D. Nikapota* 743

Lecture

Dangerous mistakes. *N. Walker* 752

Papers

Unexplained fluctuations in the risk for schizophrenia by month and year of birth. *R. E. Kendell and W. Adams* 758
Season of birth in schizophrenia. Evidence for confinement of an excess of winter births to patients without a family history of mental disorder. *E. O'Callaghan, T. Gibson, H. A. Colohan, D. Walshe, P. Buckley, C. Larkin and J. L. Waddington* 764
The clinical correlates of neurological soft signs in chronic schizophrenia. *D. J. King, A. Wilson, S. J. Cooper and J. L. Waddington* 770
Sex differences in suicidal behaviour of referred adolescents. *J. M. Rey and K. D. Bird* 776
Using the Hospital Anxiety and Depression Scale to screen for psychiatric disorders in people presenting with deliberate self-harm. *D. Hamer, D. Sanjeev, E. Butterworth and P. Barczak* 782
Treatment as an alternative to prosecution: offenders diverted for treatment. *D. J. Cooke* 785
Compulsory psychiatric treatment in the community. I. A controlled study of compulsory community treatment with extended leave under the Mental Health Act: special characteristics of patients treated and impact of treatment. *T. Sensky, T. Hughes and S. Hirsch* 792
Compulsory psychiatric treatment in the community. II. A controlled study of patients whom psychiatrists would recommend for compulsory treatment in the community. *T. Sensky, T. Hughes and S. Hirsch* 799
Day care in an inner city. I. Characteristics of attenders. *F. Holloway* 805
Day care in an inner city. II. Quality of the services. *F. Holloway* 810
The nature and severity of disabilities in long-stay psychiatric in-patients in South Glamorgan. *I. G. Pryce, R. D. Griffiths, R. M. Gentry, I. C. T. Hughes, L. R. Montague, S. E. Watkins, J. Champney-Smith and B. M. McLackland* 817
The prediction of chronic persistent versus intermittent tardive dyskinesia. A retrospective follow-up study. *W. M. Glazer, H. Morgenstern and J. T. Doucette* 822
Adoption and eating disorders: a high-risk group? *N. L. Holden* 829

Continued inside

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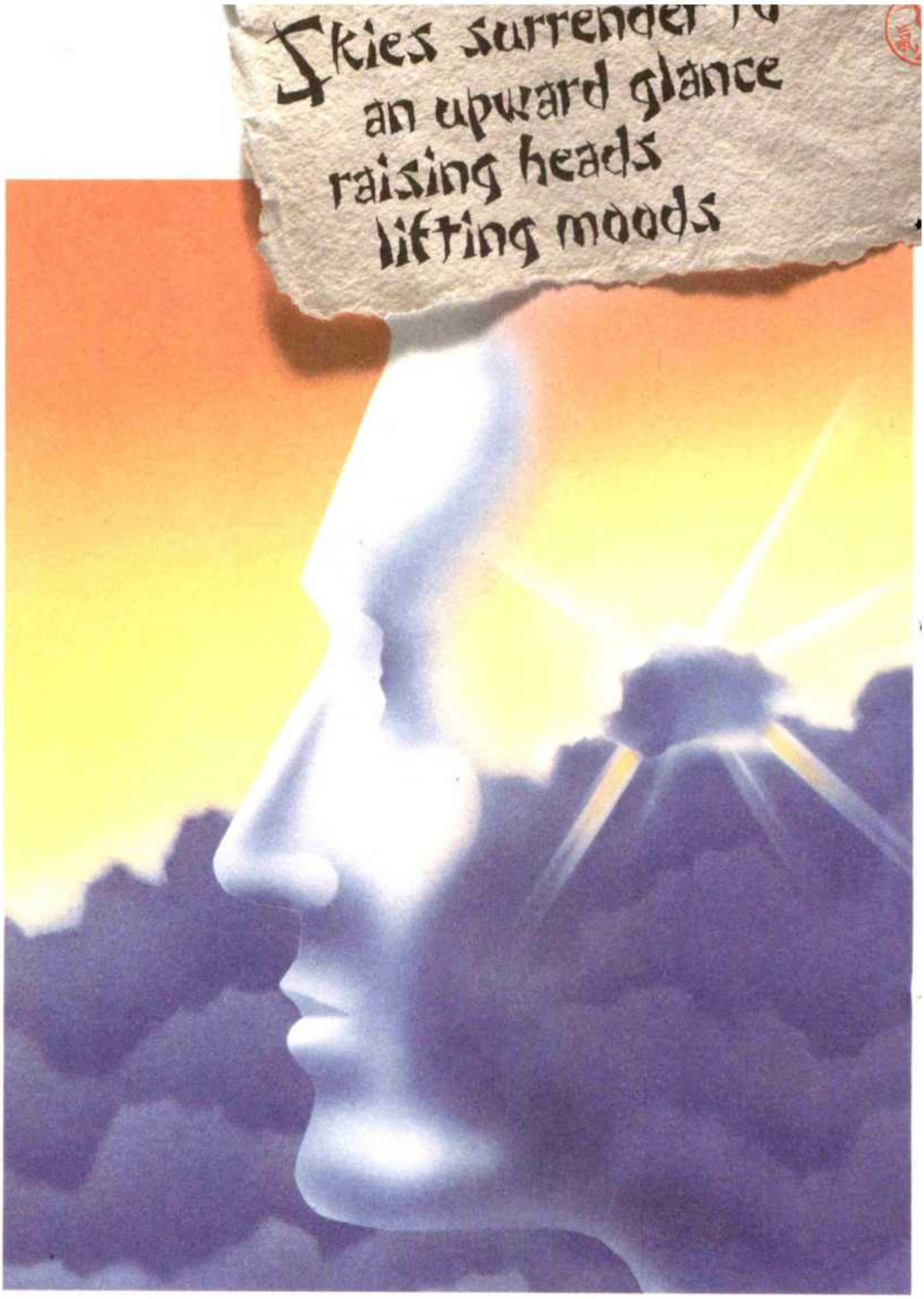

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Contents continued from front cover

The Current Literature

Is schizophrenia disappearing? *J. M. Eagles* 834

Brief Reports

Exposure therapy for post-traumatic stress disorder. Four case studies. *D. A. Richards and J. S. Rose* 836
Pattern of obsessive-compulsive disorder in eastern Saudi Arabia. *O. M. Mahgoub and H. B. Abdel-Hafeiz* 840
Polycythaemia rubra vera, cerebral ischaemia and depression. *D. Murray and R. Hodgson* 842
Successful treatment of paraphilic coercive disorder (a rapist) with fluoxetine hydrochoride. *M. P. Kafka* 844
Spontaneous improvement of tardive dystonia during mania. *O. Yazici, E. Kantemir, Y. Tastaban, A. Üçok and M. Özgüroglu* 847
Is the predisposition to neuroleptic malignant syndrome genetically transmitted? *K. Otani, M. Horiuchi, T. Kondo, S. Kaneko and Y. Fukushima* 850
No crossover reactions to citalopram or paroxetine among patients hypersensitive to zimeldine. *B-O. Bengtsson, J. Lundmark and J. Walinder* 853
Dependence on monoamine oxidase inhibitors in high dose. *D. Vartzopoulos and F. Krull* 856

Columns

Correspondence 858
A hundred years ago. *Researched by H. Rollin* 867
Books reconsidered. *One flesh: Separate Persons* (Skynner). *S. Ruszczynski* 868
Book reviews 871
American Journal of Psychiatry (contents) 880
The Journal of Nervous and Mental Disease (contents) *facing* 880

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Annotation

The Marketing of 5-Hydroxytryptamine: Depression or Anxiety?

DAVID HEALY

The discovery that tricyclic antidepressants blocked the re-uptake of both noradrenaline and 5-hydroxytryptamine (5-HT) was a significant step on the road to the development of the monoamine hypotheses of depression (Healy, 1987). The subsequent demonstration that the de-aminated metabolites of amitriptyline and imipramine, nortriptyline and desipramine, were antidepressants tilted the balance toward noradrenaline as the pertinent neurotransmitter, as these latter drugs were clearly inhibitors of noradrenergic rather than 5-HT uptake.

In 1964, Ciba Geigy chlorinated imipramine, in an attempt to produce a more effective antidepressant. However, not only was the resulting chlor-imipramine no more effective, it seemed to be markedly more toxic (Pinder, 1987), so much so that it was only licensed by the Food and Drugs Administration (FDA, Washington, DC) for use in the USA in 1990.

During the 1970s, Astra consulted Arvid Carlsson regarding the development of an antidepressant. He noted that, although a rational appraisal of the situation might suggest that desipramine and nortriptyline must be the core tricyclic antidepressants, clinicians appeared to prefer amitriptyline and imipramine (Carlsson, 1990). He pinpointed 5-HT re-uptake blockade as the effect that tertiary amine tricyclics have which their metabolites do not, and suggested accordingly that drugs specific for 5-HT re-uptake inhibition should be developed and tested for antidepressant efficacy. Clomipramine, then the most specific 5-HT re-uptake inhibitor, was used as a basis to design zimelidine, which was marketed in the early 1980s. Clinical trials suggested that it was an antidepressant but it was later withdrawn because of side-effects. Since then other 5-HT re-uptake inhibitors have followed.

Meanwhile, given the dominance of amitriptyline and imipramine in clinical settings, Ciba Geigy were faced with a marketing problem for clomipramine. They produced a parenteral preparation of clomipramine and encouraged prescribers to look at alternative indications. This led to its being given in large doses intravenously in a number of single-blind and non-placebo-controlled studies for phobic and obsessional states (for review see Healy, 1990). It appeared to be in some way anxiolytic – if anything more anti-phobic than anti-obsessional. However, the market for phobic/anxious depressions was at this time targeted by producers of monoamine oxidase inhibitors (MAOIs), whose sales had slumped as a result of both the MRC comparative trial of antidepressants in 1965 and the recognition of the 'cheese effect'. Clomipramine was subsequently marketed as anti-obsessional and it was for this indication that it was licensed by the FDA in 1990.

Whether the promotion of clomipramine as anti-obsessional was as market orientated as this analysis may suggest is uncertain, but the outcome today is that it and other 5-HT re-uptake inhibitors are marketed as specific for obsessive–compulsive disorders (OCD). It has been suggested that a large part of this impression derives from the fact that drugs which block 5-HT re-uptake are almost the only ones to have been studied properly in OCD (Marks *et al*, 1988). There has not been, for example, a proper study of neuroleptics in OCD, although prior to the introduction of clomipramine, neuroleptics appear to have been the standard treatment for OCD.

While there is some dispute about just how useful clomipramine is in OCD (Marks *et al*, 1988), there is an emerging consensus that it, and other 5-HT re-uptake inhibitors, in contrast to the non-5-HT re-uptake inhibiting antidepressants, are of some use. Are 5-HT re-uptake inhibitors then in some way anxiolytic rather than, or in addition to, being antidepressant? To try and focus further on this issue, I consider firstly the evidence in favour of a necessary action of antidepressants on 5-HT systems, and secondly the likely profiles of action of a number of recently developed 5-HT receptor agonists and antagonists.

Antidepressants and 5-HT

By the mid-1980s increasing interest had developed about a possible role of 5-HT receptor functioning in depression. There were several reasons for this. Firstly, it had been shown that antidepressant-induced changes in adrenergic receptors did not take place, unless there was an intact 5-HT system (Sulser, 1984). Secondly, antidepressant treatment was shown either to sensitise post-synaptic 5-HT_2 receptors (De Montigny *et al*, 1988; Healy *et al*, 1985) or to influence receptor number (Cowen *et al*, 1986). Thirdly, it was also known from animal work that lithium has pre-synaptic effects on the 5-HT system and sensitises post-synaptic 5-HT receptors (Price *et al*, 1990). In an attempt to study this effect in humans, De Montigny *et al* (1981) and Henninger *et al* (1983) added lithium to the tricyclic antidepressant regimes of treatment-resistant depressives and reported a rapid and remarkable improvement in mood. This was put down to the ability of lithium to sensitise 5-HT_2 receptors, with the implication that effective antidepressant treatment in general worked by this means (De Montigny *et al*, 1988).

Finally, based on this effect of lithium, a variety of treatment cocktails have been developed; the most notable of these have been the combinations of clomipramine, L-tryptophan and lithium (Hale *et al*, 1987) and phenelzine, L-tryptophan and lithium (Barker *et al*, 1987). A common feature of these regimes has been an attempt to selectively influence the 5-HT system (Leonard, 1988). The recent withdrawal of L-tryptophan from the market has led, it would seem, to a number of patients on such regimes relapsing (Ferrier *et al*, 1990).

It is, however, far from certain that there is any specific effect of manipulating the 5-HT system in treatment resistance. It is almost impossible to compare adequately the addition of lithium to the effect of adding another antidepressant or neuroleptic to an apparently ineffective regime. The initial claims in favour of lithium did not capture attention by virtue of any proven specificity to the 5-HT system or even to treatment resistance, but rather by a seemingly dramatic induction of clinical change – within 48 hours. This in turn appears to have done more than anything else to confer the impression of specificity to the 5-HT system. Such rapid responses are not now cited and would seem to have been a chance phenomenon.

In one of the largest studies of treatment resistance Shapira *et al* (1988) gave clomipramine and/or lithium to a group of 12 electroconvulsive therapy-resistant depressed subjects but found that the mean time to recovery was 2.2 months. Such delay hardly suggests a specific role for manipulations of the 5-HT system. Reviewing all studies in the area, Price (1989) has recently concluded that lithium augmentation brings about a response in around 50% of cases and that the mean time to response may be about three weeks. This suggests that there may be little difference between adding lithium to an ineffective regime or adding another antidepressant, such as mianserin, or a judicious dose of a neuroleptic.

Treatment-resistant subjects are also a difficult group from which to extrapolate. It can perhaps be noted that what in effect was the first study of lithium augmentation was conducted by Lingjaerde *et al* in 1974, on 45 clearly endogenously depressed subjects, who were randomly given a tricyclic antidepressant and lithium or a tricyclic antidepressant and placebo. They concluded that lithium appeared to enhance the effects of tricyclic antidepressants but the differences between lithium and placebo groups were not significant.

5-HT receptor agonists and antagonists

The initial monoamine depletion hypotheses gave way in the late 1970s to a variety of adrenergic receptor hypotheses, notably the alpha-2 supersensitivity and the post-synaptic beta receptor supersensitivity hypotheses (Healy, 1987). Comparable hypotheses, implicating 5-HT receptors, were held up by technical difficulties in identifying receptor subtypes.

In 1979, using radioligand binding methods, Peroutka & Snyder distinguished between a 5-HT_1 and 5-HT_2 receptor. The development of selective agonist and antagonist radioligands to further distinguish between 5-HT receptor subtypes has subsequently produced a profusion of new receptor subtypes. Some of these experimental compounds have been successfully refined further for use in man. It is with the behavioural profile of these latter drugs that we are now concerned.

From Table 1 it will be clear that there is some overlap between the 5-HT_{1c} receptor and the 5-HT_2 receptor; it seems likely that these may in future be designated as 5-HT_{2a} and 5-HT_{2b}. A 5-HT_{1b} receptor exists only in animals. A 5-HT_{1d} and 5-HT_4 receptor have been proposed but at

Table 1
5-HT receptor agonists and antagonists

	Agonist	Antagonist
5-HT_{1a}	8-OHDPAT Buspirone Gepirone Ipsapirone Flesinoxan	Methsergide Spiperone Propranolol
5-HT_{1c}	mCPP	Ritanserin Mianserin
5-HT_2	d-LSD	Ketanserin Ritanserin Risperidone Mianserin Trazodone All neuroleptics
5-HT_3	2-methoxy-5-HT	Ondansetron Granisetron Zacopride

This table is based on the guidelines of the serotonin receptor club nomenclature committee, December 1989.

present remain radiolabelled binding sites only, without an obvious functional correlate (Peroutka, 1988; Gonzalez-Heydrich & Peroutka, 1990).

If the antidepressant action of 5-HT re-uptake inhibitors is mediated through the 5-HT system – it is not a foregone conclusion that this is necessarily the case – then presumably this must be effected indirectly by altering the availability of 5-HT to one or other of these receptors. If 5-HT has a role in either depression or anxiety, it might be expected then that drugs acting more directly on one or other of these receptors would be either clearly anxiolytic or antidepressant.

5-HT_1

The picture as regards drugs active at the 5-HT_1 site is complex. The recently introduced buspirone, which is a partial agonist for the 5-HT_{1a} site, has been marketed as an anxiolytic. Since its introduction a number of more specific agonists for this site have been developed – ipsapirone, gepirone and flesinoxan. These compounds all show efficacy in animal screening tests for anxiolytic compounds. They appear, however, to have a significantly different profile to the benzodiazepines, being inactive in some of the screening tests used to detect benzodiazepine-type anxiolysis (Gonzalez-Heydrich & Peroutka, 1990; Glennon, 1990).

In contrast to buspirone, however, flesinoxan and ipsapirone, which also appear in early pre-release studies to be anxiolytic in man, are currently being tested as antidepressants. One rationale offered for this stems from the finding that the prototypical 5-HT_{1a} agonist, 8-OHDPAT, potently reverses some of the behaviours in animals that constitute learned helplessness (Gonzalez-Heydrich & Peroutka, 1990). As this is a model of depression rather than anxiety, the inference drawn has been that 5-HT_{1a} agonists might be antidepressant. There are other ways, however, to interpret this switch in indications which will be developed below.

5-HT_2

In the case of the 5-HT_2 receptor, it appears that the hallucinogenic effects of LSD and mescaline are mediated through the 5-HT_2 receptor (Davis, 1987). These effects can be blocked in animals by ketanserin and ritanserin (Davis, 1987). There is also some evidence that 5-HT_2 antagonists such as ritanserin or risperidone are of benefit in schizophrenia (Gelders, 1989). All current neuroleptics, furthermore, in addition to having common actions on D-2 receptors, also block 5-HT_2 receptors (Glennon, 1990). The difference between their actions on these two receptor systems is that the doses used clinically for the different neuroleptics correlate closely with their ability to bind to D-2 receptors, whereas this is not so in the case of their binding to 5-HT_2 receptors.

The presence on this list of mianserin and trazodone, which have both been marketed as antidepressants, is of interest. In the case of mianserin, however, this agent also has a significant effect on adrenergic receptors. In the case of trazodone, of interest is the fact that one of its derivatives – mCPP, which is an agonist for the $5\text{-HT}_{1c}/5\text{HT}_{2b}$ receptor – is potently anxiogenic (Zohar *et al*, 1988).

5-HT_3

Several years ago, it appeared that 5-HT_3 receptor antagonists might be effective in schizophrenia, based on tests in animal models of schizophrenia (Costall *et al*, 1988). This led to the development of a number of compounds such as Glaxo's ondansetron, Smith Kline Beecham's granisetron and others which are shortly due to come onto the market. It has since become clearer that 5-HT_3 receptor antagonists have an anxiolytic profile that differs from that of both benzodiazepines and 5-HT_{1a} agonists (Jones *et al*, 1988).

Of particular note is that 5-HT_3 receptor antagonists appear, in animals, to reverse effectively the anxiety that is induced by benzodiazepine discontinuation (Costall *et al*, 1990).

The marketing of 5-HT

In addition to perhaps 20 to 30 new 5-HT re-uptake inhibitors, there are a great number of new compounds, with relatively specific actions on the 5-HT system, that have begun to appear on the market. Are they anxiolytic or antidepressant or both? The overview, above, of the behavioural effects mediated through 5-HT receptors suggests that 5-HT has more to do with anxiety than depression. This, however, is an issue that is likely to be confounded greatly by the efforts of drug companies to market their products.

For example, the relative failure of buspirone to make major inroads in the marketplace suggests that it will be very difficult to market a general anxiolytic, in the post-benzodiazepine era. Such a compound would have to be both as effectively anxiolytic as the benzodiazepines and remarkably safe. The safety factor comes into play when one considers that broad-spectrum anxiolytics may end up being prescribed for substantial sections of the population, so that the potential liability to the company should anything go wrong is considerable.

This must be one reason why so many 5-HT re-uptake inhibitors are being produced – and why the temptation to market them as antidepressants is all but irresistible. These compounds can be produced easily. They are far safer than the earlier tricyclics and MAOIs. They are so safe that it becomes a feasible proposition to take the current findings from social psychiatry and advise general practitioners that there are many more untreated depressives than was formerly thought; often conditions presenting as anxiety stem from an underlying depression, and current evidence suggests that antidepressants (in contrast to anxiolytics) need to be taken chronically, in order to reduce the risk of relapse. Marketing as antidepressants also produces a different (and more useful) set of expectations in both prescribers and consumers – that the drugs will not do much in the short term. There is, therefore, a good marketing rationale for producing 5-HT re-uptake inhibiting 'antidepressants'. From the beach-head of depression, raids can subsequently be launched on the hinterlands of anxiety, following the well-established precedent of the MAOIs and clomipramine.

Are 5-HT re-uptake inhibitors, therefore, not antidepressant? Currently in clinical trials for antidepressants, the Hamilton Rating Scale for Depression (HRSD) is the most commonly used instrument. A problem with the HRSD is that a considerable part of the total score may derive from questions that are concerned with anxiety. An effective anxiolytic agent may substantially reduce total scores and such reductions are then often uncritically interpreted as evidence of antidepressant efficacy.

On this basis all neuroleptics have been 'shown' to be antidepressants (Robertson & Trimble, 1982). Lundbeck, in particular, have conducted a successful marketing campaign for flupenthixol, using such data to suggest that it is in someway both a neuroleptic and an antidepressant (for review see Healy, 1990). Both diazepam and alprazolam have comparable antidepressant credentials (Tiller *et al*, 1989; Rickels *et al*, 1985); the companies concerned have, however, had other marketing targets (Healy, 1990).

Many of the more recently developed compounds active at 5-HT receptors will also provide substantial benefits for depressed patients as rated by the total Hamilton scale score. The 5-HT re-uptake inhibitors do just this. Are such agents specifically antidepressant? Against this possibility is the fact that there is no relationship between potency in inhibiting 5-HT re-uptake and antidepressant efficacy. Indeed, the recently developed and apparently antidepressant tianeptine appears to promote 5-HT uptake (Fattacini *et al*, 1990). It must be remembered as well that the original of the species, clomipramine, had a much wider range of actions than the more specific compounds currently being introduced.

There is a further possibility. It appears that there is a substantial overlap between the 5-HT and dopaminergic systems. Both 5-HT_3 receptor antagonists and D-2 receptor antagonists are antiemetic (Costall *et al*, 1988). Neuroleptics, 5-HT re-uptake inhibitors and 5-HT_{1a} agonists increase prolactin levels. Both neuroleptics and fluoxetine have been reported to produce akathisia (Lipinski *et al*, 1989). 5-HT_{1d} receptors are found principally in the basal ganglia (Peroutka, 1988). 5-HT_3 receptor antagonists modulate mesolimbic dopamine release (Tricklebank, 1989). There are grounds, therefore, to believe that drugs active on the 5-HT system may modulate dopaminergic systems or vice versa.

Of note here is the fact that the first report of a possible benefit of clomipramine in OCD suggested that it helped by producing a state of indifference to intrusive thoughts and imagery (Cordoba & Lopez-Ibor, 1967; Healy, 1990). I have argued, elsewhere (Healy, 1989), that the beneficial effects of neuroleptics also follow from the induction of a state of psychic indifference – although one that appears to come on far more rapidly than that induced by clomipramine, albeit with the drawback of being often accompanied by counterproductive side-effects. Without more precise phenomenological descriptions from patients, it is not possible to say whether these effects differ, other than in the time course of their onset.

A case can be made therefore that manipulating 5-HT functioning may, in certain circumstances, be indirectly neuroleptic. On this basis, current cocktails for treatment-resistant depressions, which manipulate 5-HT systems, may be equivalent to adding a neuroleptic to an established antidepressant regime.

The way forward?

When new compounds are produced, there is a *prima facie* case for conducting a series of open studies in clinical populations to establish their actual effects in man as opposed to the effects proposed by current theories or by extrapolation from animal experiments. This, however, is not the way the modern pharmaceutical industry works.

The production of a drug requires a prior determination of market returns balanced against liabilities. This initial requirement tends to act as a mould into which subsequent developments must be fitted. This will often apparently lead to companies ignoring information about unexpected clinical benefits which might complicate the figures. A recent example concerns calcium-entry blocking agents (Healy, 1990). Company information, until recently, suggested that these agents do not cross the blood–brain barrier. However, it was observed that such agents may ameliorate tardive dyskinesia (Barrow & Childs, 1986), an observation subsequently replicated, which has not, it would seem, been taken up and promoted by the companies concerned. This is presumably because the balance-sheet of gains and liabilities might be incalculably disrupted by doing so.

This example of clinicians noting the effects of a drug on a condition other than the one it was prescribed for contains an important pointer. To date, all significant developments in psychopharmacology have happened serendipitously (see Sneader, 1990; Kuhn, 1990; Sandler, 1990 and for review Healy, 1990). None have been the result of a double-blind placebo-controlled study. At present, the interpenetration of psychopharmacology with the pharmaceutical industry, although of immense benefit in many respects, tends to obscure this and to suggest instead that all the significant research has been done before a drug comes to the marketplace – apart from the formality of a set of clinical trials. This is simply not the case. All too often the clinical trial, today, merely sets the seal on a marketing process rather than acts an independent piece of research.

Clinicians need to research 'independently' the effects of these new compounds. We need also to come up with operational criteria for antidepressants (and other psychotropic drugs), so that simply achieving effects in clinical trials cannot be passed off as evidence that the drug in question is an imipramine-equivalent, for example. There are a number of recent developments that perhaps may help in this. One has been the development of rating scales, such as the Montgomery-Asberg Depression Rating Scale (MADRS), which are much less likely to throw up false positives with anxiolytics.

Another is the development of multiple-baseline methods, which could potentially replace the placebo-controlled trial (Kazdin, 1982). Such methods would permit studies on small numbers of patients rather than the hundreds needed for adequate placebo-controlled studies. These smaller numbers could then consist of clearly endogenomorphically depressed subjects; the kind of individuals who would seem least likely to respond to an anxiolytic.

Finally, Quitkin *et al* (1984) and Kravitz *et al* (1990) have suggested that a true antidepressant response can be differentiated on the basis of a pattern analysis as opposed to a consideration of overall success rates compared to placebo. A clear delay in response of up to two weeks has traditionally been taken to be characteristic of antidepressants as opposed to anxiolytics or neuroleptics. Ironically, this may indicate the best basis for claiming that the 5-HT$_{1a}$ agonists are antidepressants, in that response to these compounds takes two to three weeks to appear.

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British Journal of Psychiatry (1991), **158**, 743–751

Review Article

Child Psychiatry in Developing Countries

ANULA D. NIKAPOTA

Child psychiatry in developing countries has recently attained the status of an established specialty. This review looks at available epidemiological data, and factors contributing to similarities and differences in rates of disorder. The relevance of child psychiatry to child health in these countries has service, training and research implications.

Significant growth in child psychiatry in developing countries has occurred only in the last 20 years despite the fact that children under 15 years of age constitute 40–50% of the population of these countries. Evidence of the substantial morbidity arising from mental health problems and of the significance of psychosocial factors to childhood morbidity has, however, only recently become available. An earlier review points out that to recognise the needs of children with maladaptive behaviour, an understanding of local developmental and child-rearing practices is required, which is difficult for psychiatrists trained within Western cultures (Minde, 1976). Scarce resources have been used to combat major causes of childhood mortality and morbidity; since child psychiatry was not considered relevant to these concerns it was accorded low priority (Olawatura, 1978).

Developing countries all share certain features. They are, by definition, less industrialised than developed countries, with limited resources for service development. Populations are relatively young and often predominantly rural. Many countries have established traditional cultures which affect beliefs and life-styles. Changes in traditional values due to economic, political, and educational influences lead to considerable diversity within and between countries. There are, nevertheless, many areas and issues of common interest with regard to child psychiatry, which are relevant also to the discipline as a whole. This review will focus on these issues in relation to firstly the epidemiology of child psychiatric disorders and secondly the development of child psychiatric services.

Epidemiological Issues

The importance of epidemiology is related to demonstrating presence of, and need for services for, mental health problems, the relevance of these problems to major causes of mortality and morbidity such as malnutrition and infections, and the identification of causal links and preventive measures (Graham, 1980). There are few data from community-based epidemiological studies compared with developed countries. However, sufficient evidence does exist to demonstrate significant morbidity from child psychiatric disorders. Surveys in Ethiopia (Giel *et al*, 1969), the Sudan (Baasher & Cederblad, 1966), and India (Lal & Sethi, 1977) reported prevalence rates ranging from 3% to 11%, for children and adolescents. Disorders identified included emotional and behaviour problems, developmental delays, psychosis, mental retardation and epilepsy with associated behaviour disturbance.

A four-country study done in primary health-care settings in the Sudan, Columbia, India and the Philippines (Giel *et al*, 1981) gave a prevalence rate which varied from 12% to 29% for child psychiatric disorders. A major reason for differences in reported rates at the different sites was consultation patterns for children with mental retardation and associated behaviour problems. Mental retardation is part of the child psychiatric case load in developing countries. Prevalence rates are in the region of 8–12 per 1000 children aged between three and ten years (Narayanan, 1981; Belmont, 1984; Tao, 1988).

Controlled studies of school children in the differing situations of urban Uganda (Minde, 1975), Beijing (Yu-Feng, 1989), and Hong Kong (Luk *et al*, 1988) have demonstrated that the rate of behaviour problems in school children approximates very closely to rates of disturbance reported from studies in developed countries. World Health Organization (WHO) case studies done in a number of countries which included Egypt, Nigeria, India, Indonesia, Thailand and Sri Lanka illustrated that child psychiatric symptomatology does not differ to a significant extent across cultures. Findings from these case studies also demonstrated that culture-specific disorders are very rare among children.

There may be cross-cultural differences, however, in symptoms or behaviour which initiate help-seeking behaviour. A multi-centre study in SE Asia found that 10–15% of children presenting with somatic symptoms had functional complaints

(Sell *et al*, 1988). Parents are anxious about physical illness in childhood and accustomed to seeking treatment for such problems. Paediatric clinic populations include a significant number of children with mental health problems (Singh *et al*, 1989). Child psychiatric clinic data highlights parental and community concerns and reflects perceptions of need. Certain common features can be observed in data from clinic populations (Minde, 1977; Indian Council for Medical Research, 1982; Nikapota, 1983). Children with mental retardation form a substantial proportion of those seen, and are easily identifiable. Many local languages have a specific term for mental retardation. Help-seeking behaviour is associated with the recognition of this condition whether from a traditional healer, indigenous medical practitioner or Western-trained doctor. Expanding educational services have led also to the identification of children with learning disorders who are presented as lazy or disinterested in study. Children with emotional and neurotic disorders are commonly seen. Hysterical disorders are probably more common than in developed countries, but conduct disorders rarely present. Difficult behaviour is not perceived as requiring help or treatment but rather as a situation requiring advice or discipline. Help may be sought from family elders or community leaders, rather than health facilities.

Children seen at clinics often do not have psychiatric problems, reflecting parental anxieties and differing perceptions of abnormality (Bose & Goh, 1979). The author found a number of normal young children with a stammer being brought because of anxiety that the stammer predicted 'brain' problems (Nikapota, 1983).

Adolescents with depression and psychosis may present more commonly to adult psychiatric facilities. Available information indicates that schizophreniform psychosis may be more common among adolescents from Asia and Africa than in Western cultures. An emerging problem among adolescents, causing high levels of concern among families and communities, is experimentation with, and addiction to, dependence-producing drugs. The magnitude of the problem varies enormously from country to country, from 16% in Kenya (Dhadphale *et al*, 1982) to an estimated 43% in Colombia. Anorexia is rare and reported particularly in adolescents from middle- and upper-class families (Al-Ansari & Shubar, 1987; Buhrich, 1981; Parry Jones, 1986). Adolescents who have attempted suicide rarely present to out-patient facilities, often because of social or religious taboos or legal sanctions which are in force for attempted suicide (Dissanayake & De Silva, 1974; Sathyavathi, 1975).

Factors contributing to differences in rates of child psychiatric disorders

Findings quoted above indicate that patterns of child psychiatric disorder and prevalence are similar across cultures, lending validity to the current practice of using common criteria and classification systems. It could be argued that differences in rates reflect variations in the influence of predisposing or protective factors in the respective communities or cultures. It is also possible that current diagnostic criteria do not always permit identification of disorder in particular cultural contexts although evidence so far suggests that significant differences do not occur.

Organic factors

Evidence of the relative role played by organic as opposed to environmental factors is insufficient except in the case of mental retardation where the role of preventable organic factors has been demonstrated through clinic data as well as community-based studies (Hasan & Hasan, 1981; Narayanan, 1981; Belmont, 1984). The association between levels of cognitive development and conditions such as non-acute malnutrition (Chavez & Martinez, 1982) or anaemia (Agarwal *et al*, 1989) highlights the need for further study on the effect of organic factors on the child's ability to interact with and make demands from its natural environment.

Individual and environmental differences

Age, sex, and urban or rural setting are commonly associated with differences in rates in a manner which is similar across cultures. This has been observed in studies from Uganda (Minde, 1975), Hong Kong (Luk *et al*, 1988), Nigeria and the Sudan (Cederblad, 1988), Thailand (Weisz *et al*, 1987) and China (Yu-Feng *et al*, 1989). Findings have been comparable with those from Sweden (Cederblad, 1988) and the United Kingdom (Rutter *et al*, 1975). Conduct disorders are commoner in boys and neurotic disorders in girls, incidence increasing with age. It would appear that the mechanisms by which individual differences in children modify responses to environmental experiences may be stable across cultures. Cultural factors may play a part in determining how experiences lead to a facilitatory or potentially maladaptive response from a child according to age, sex or differences such as position in family. Multiparity is an established risk factor, irrespective of age and sex. Younger children are more vulnerable in situations where the traditional caring patterns do not include attempts to help young children adapt to or understand change. In some cultures, family responsibilities seem to contribute to an increased vulnerability in the eldest son (Al-Issa, 1989).

The higher rates observed in urban samples may indicate that influences of urban living increase the vulnerability of children, despite possible advantages such as easier access to health care and educational facilities. This effect has been observed even where traditional support systems have been preserved during the rural to urban transition (Rahim & Cederblad, 1984). Differences in family life-style and employment patterns; changes in parental expectations, and attitudes to and tolerance of behaviour; educational and academic pressures; and an increased level of family stress, are all factors related to urban living that have been implicated as causing increased rates of disturbance in children (Minde, 1975; Giel *et al*, 1981; Rahim & Cederblad, 1984).

Family factors and child-rearing practices

There has always been an assumption that the extended family is protective with regard to emotional and behaviour problems in children, particularly where surrogate parenting is required due to separation from parents, or marital disruption. This was reflected in case-study reports from a number of countries (Sartorius & Graham, 1984) and in studies in the Sudan and Nigeria (Cederblad, 1988), and China (Yu-Feng, 1989). On the other hand, intergenerational conflict of values can be associated with a higher rate of problems (Minde, 1975; Kong *et al*, 1988). Both negative and positive effects of the extended family have been observed clinically. A study on the vulnerability of the nuclear family has been done in China with particular reference to the one family, one child policy; evidence so far does not indicate that this practice has undesirable psychological sequelae (Tseng *et al*, 1988).

Marital conflict, separation and divorce are associated with increased problems in children (Sartorius & Graham, 1984). Separation or divorce may lead to social isolation of a mother or disruption of extended family networks. Clinically, these mothers are often observed to be depressed, leading to poor levels of care for their children. Recent work in SE Asia which looked at risk factors for child mental health and development found a significant association between social isolation, poor levels of care and increased risk of developmental delays (World Health Organization, 1989).

Despite significant degrees of socio-economic deprivation and morbidity from physical disease, rates for non-organic child psychiatric disorder appear to be no greater in developing countries than developed countries. Previous beliefs that children are exposed to less stress, or that the extended family functions as a protective mechanism cannot be considered valid explanations. It is important for developing countries to identify facilitatory as well as maladaptive mechanisms within current child-care patterns. Strengthening potentially facilitatory practices and community education to alter potentially maladaptive ones is a part of primary prevention. Close physical contact with mother from infancy is cited as one positive factor (Cederblad, 1988), but a protective function cannot invariably be assumed for the close physical contact which is often a part of child-care practice. In the author's experience the benefit of this contact depends on the quality of the carer's responsiveness and sensitivity to the needs of the child she is carrying around. This view is also expressed in a paper reviewing causes of morbidity in pre-school children in Indonesia (Humris & Saputro, 1985).

Recent work on the relevance of caring styles and feeding practices, not only to early child development, but also to important physical health problems in the young child such as malnutrition, has highlighted the importance of bonding and a responsive carer–child interaction (Cravioto & DeLicardie, 1976; Choudhry & Rao, 1983; Heptinstall *et al*, 1987).

Carers often do not appreciate the degree to which children react to events within a family, or the child's need to express these feelings. Families may behave in a way that denies, rather than acknowledges, the event and the feelings aroused, to reduce distress in the child. This practice is clinically associated with problems in children. For example, sibling rivalry is acknowledged by parents but children are often actively discouraged from expressing these feelings, which are considered socially inappropriate. Sibling rivalry leading to behaviour problems is commonly encountered clinically. Conflicting reports of the effect of parental involvement with education have been given. Yu-Feng *et al* (1989) found that parental involvement was associated with fewer problems in school-age children, but the same factor often presents clinically in SE Asia as leading to problems.

Controls and disciplinary practices are an area of caring which is influenced by socio-cultural factors and has a significant impact on parent–child relationships. Parents seem to have a common yardstick for rating behaviour as desirable or undesirable (Honig & Chung, 1989). Attitudes to physical punishment as a negative reinforcer vary; where widely used it may be the commonest form of physical abuse in a country (Wilson-Oyelaran, 1989). Associations between conduct problems and physical punishment of the child (Minde, 1975) may be due to the fact that conduct problems are perceived as requiring discipline, or alternatively could be of significance in leading to the problem in the child.

Socio-cultural factors, attitudes and perceptions

Socio-cultural values, attitudes and circumstances may lead to differing rates of disorder. It is accepted that the relative rarity of anorexia except among middle-class adolescents could be due to the value accorded to food in cultures where sufficient food is a luxury. Culture-bound fears about aspects of sexual development such as masturbation and nocturnal emission have been associated with anxiety disorder in adolescents (Dissanayake, 1981). Mention has been made of clinical data which indicate that functional complaints may be commoner in cultures where there is pressure on children and adolescents to conform to social norms. Cultural norms with regard to behaviour do alter rates of observed behaviour problems, as reported in a cross-cultural comparison of Thai and US children (Weisz *et al*, 1988). The role of the peer group is an area which has not yet been sufficiently explored. In many Asian cultures, peer-group influence may be less than in Western cultures. Peer-group support was a protective factor identified in a study of Colombian street children (Aptekar, 1989).

Rates presenting at health facilities will be affected by attitudes and perceptions of the need for help. Higher educational levels among parents was one of the factors significantly associated with attendance at a clinic for learning disabilities in Kenya (Resnick *et al*, 1988). The author found, however, that education was not always associated with greater understanding of a child's problem, since education was also associated with higher and less flexible expectations with regard to the child.

It is of interest to note that there is considerable common ground across cultures in relation to children's perceptions of stress, despite differences in cultural background and upbringing. Academic stress is commonly associated with school refusal and a variety of functional complaints including the 'brain fag' syndrome (Nikapota, 1981; Okasha *et al*, 1988). Both the low and high achievers have been observed as being vulnerable. The latter group become vulnerable because of personal and family expectations of high achievement. A cross-cultural comparison of children's perception of stress found that certain stresses such as loss of a parent are universally rated as stressful. Experience did, however, affect the children's perceptions of certain situations. For example, blindness was rated as more stressful by children in communities where this was a common phenomenon. The World Health Organization case studies referred to earlier found that stress factors identified were similar to those in developed countries and included academic stress, separation from parents, marital conflict or disruption, and bereavement (Sartorius & Graham, 1984).

Risk groups

Child abuse is an issue of concern which in developing countries has received relatively little attention. There is often a belief that abuse does not occur. This is not so, although the availability of the extended family as well as the relative lack of privacy within families may serve as a protection against physical abuse of the baby or young child. Deliberate neglect of unwanted children because of illegitimacy or severe disability has been known. There is some evidence from a study in Hong Kong that the group at risk of abuse are older children (Lieh-Mak *et al*, 1983).

There has been little systematic study of sexual abuse although it is known that incest involving adolescent children does occur in many communities. Major problems of abuse rise from the existence of social systems such as exploitative child labour. Issues apart from poverty seem to determine family decision-making processes leading to the selection of a particular child for entry into labour, similar to the psychodynamic process which leads to the scapegoating of a particular child. Any study of abuse must, therefore, include the psychological impact of enforced work on children. The problem, and hence the risk group, is immense in some countries (Sundari *et al*, 1984; Maheswari *et al*, 1986; Wilson-Oyelaran, 1989). In the author's experience many of these children are also subject to physical or sexual abuse since they are perceived as being without rights.

Street children, and children engaged in prostitution, are identified risk groups for psychiatric morbidity (United Nations International Children's Emergency Fund (UNICEF), 1987). Delinquency is a problem where the attitudes of society, as well as legal sanctions, lead to the identification and labelling of groups of children and adolescents who may not have delinquent traits. There are some studies of this group of youngsters which have demonstrated common associated factors such as poverty, family disruptions, and loss of supportive networks. These groups are not otherwise significantly different from other disturbed but non-delinquent youngsters (Minde & Musisi, 1990).

A number of developing countries are currently faced with situations of violence and conflict due to repressive political systems or terrorist action. The cost to children of these situations is immense (UNICEF, 1989). Anecdotal reports from Mozambique and Sri Lanka, for example, indicate that the emotional problems and maladaptive behaviour displayed by these children are similar to reactions to trauma and stress observed elsewhere. The trauma occurs in most instances to children who will additionally be subject to stresses such as poverty, malnutrition, lack of education, and disruption of normal living. The critical issue for such children is not study of symptomatology but identification of meaningful interventions which may need to focus on strengthening coping skills of the child, family and community within the prevailing situation rather than on psychotherapeutic approaches for the individual child.

Services, clinical strategies, and interventions

Child psychiatry is now a recognised specialty within developing countries. There is a wide variation in the degree to which services have developed in individual countries, but services do have certain features in common. In general, child psychiatric facilities are more closely linked to adult psychiatric facilities than in the West. Services, whether state or private, are urban-based. There are few qualified child psychiatrists, and they are usually based at academic centres. The majority of children with problems are seen by general psychiatrists or clinical psychologists. A significant proportion of the population does not have access to facilities either because it is predominantly rural or because the state-run specialised services are too expensive (Sartorius & Graham, 1984).

Clinical work includes management of the range of child psychiatric disorders seen elsewhere, but also includes the management of children with developmental disabilities and impairment, including mental retardation. Epileptic children may also present. The case load seen will, to some extent, depend on the availability of, and liaison with, other specialties such as paediatrics and neurology. Clinical practice and orientation often reflect the colonial or political links of the country (Minde, 1976; Al-Issa, 1989).

There has been no systematic evaluation of the validity of using clinical techniques developed in a very different cultural situation, nor have guidelines been developed to facilitate the adaptation or development of culture-appropriate techniques. This is currently an *ad-hoc* procedure. Clinicians need to be sensitive to the differing backgrounds, attitudes and experiences which may influence expectations and behaviour of children and their families.

Available information indicates that clinicians follow similar principles governing history-taking and assessment as are used elsewhere. Principles such as obtaining information from a number of sources and interviewing carer as well as child, have a clear cross-cultural applicability, although interviewing styles may have to differ according to background of child and family. Parents may find it difficult to discuss family problems with a professional whom they view as an outsider, or in front of their children. Where cultural values or beliefs lead to resistance, clinicians need to develop strategies to overcome them, since imposition of an alien approach will only lead to loss of contact with the family. Children may require help to express feelings about family factors, particularly in cultures where the verbalising of such opinions by children is considered very inappropriate. Drawing and giving a rank order to family members were observed by the author to be helpful in obtaining this information. Play materials need to be meaningful in relation to the child's background and experience.

The range of therapeutic interventions used in centres in developing countries will depend very much on available resources. Well-resourced centres will use a similar range of techniques to those employed elsewhere. Family therapy, as practised in clinics in the UK, is not widely used. Principles governing analysis of family function can usefully be applied for diagnostic formulations and planning of interventions. There are no systematic evaluations of the effectiveness of therapeutic approaches used, but some case reports are available. There are certain factors which influence the choice of treatment and outcome. Parents often expect a particular treatment such as medication, as this is associated with Western medicine and is popularly equated with quick results. Compliance with therapy which involves behaviour change may be affected if adequate explanation and reassurance is not given by the clinician. Many parents may find frequent clinic attendances difficult to maintain due to economic factors; families may have to travel considerable distances and cope with difficult transport conditions (Krahl *et al*, 1981). Many strategies currently employed as effective, such as the bell and pad for enuresis or stimulants for hyperactivity, can only be made available or used appropriately in well-resourced urban clinics. Finally, the professional may have to contend with a lack of support services, which limits therapeutic outcome. A practice of defining achievable therapeutic outcomes may need to be adopted. For example, in the absence of remedial education for learning problems, the therapist may have to be content with preventing or reducing associated emotional problems by working with parents to provide supportive attitudes at home for the child. Such limited outcome is, however, helpful and worth achieving.

The identification and evaluation of effective strategies in child psychiatry is far from satisfactory. There are few effective treatments for specific conditions, or criteria developed to guide clinicians in the selection of the best mode of treatment (van Engeland, 1989). The absence of clear guidelines for the choice of effective and feasible treatment approaches and the presence of the constraints already mentioned often lead to the use of inappropriate treatments. Anecdotal information leads to the conclusion that medications such as anxiolytics for school refusal and neuroleptics for a hyperactive or retarded and restless child are used more widely than is necessary or appropriate.

Epidemiological data serve to highlight need. The prevalence of morbidity in developing countries is similar to that in other countries. The coverage currently afforded by child and general psychiatrists together is one psychiatrist for populations varying from 500 000 to 3 000 000. In contrast, standards set for the UK are for two child and adolescent psychiatrists per 200 000 population in addition, of course, to general psychiatrists (Royal College of Psychiatrists, 1983). Child psychiatric expertise in developing countries may, therefore, have to be deployed differently in order to have relevance for the mental health needs of children.

Child psychiatry and services for child mental health

The value of mental health services which draw on available specialist resources for the development of mental health skills and programme activities at a primary-care level has been acknowledged. A review of some of these programmes from China, Brazil, Chile, Honduras, and India (World Health Organization, 1984) found that children with mental health problems were recognised as part of the case load for these services. The WHO collaborative study on extending mental health care (Giel *et al*, 1981) provided answers to important questions such as how, where and by whom problem children could be identified at a primary-care level.

Primary-care services for child psychiatry are better regarded as services for child mental health. There is considerable validity in integrating these services with existing services for child health (WHO, 1977). The child's needs and health status will then be considered as a whole, which facilitates primary prevention, and promotion of healthy development. Existing constraints to a better understanding of children's needs, such as a lack of consistent content on child development in training in child health within primary care (Gonzalez, 1978), will be reduced by this approach. There have been several initiatives in this direction focusing on the introduction of mental health skills into child health services or schools. One such example is a child mental health programme initiated in Sri Lanka several years ago (Nikapota, 1983; De Silva *et al*, 1988). Defined tasks relating to the promotion of healthy development and identification of children with mental health problems were introduced into primary-care services for children. Child psychiatric expertise contributed to the development of a variety of inputs of preventive or promotive relevance, development of strategies for intervention for children with problems, and training of primary-care personnel.

Therapeutic interventions based in schools are one way of extending help to children. The Newcastle study demonstrates the effectiveness of psychotherapy and behaviour therapy in the school setting and provides valuable guidelines for similar work in developing countries (Kolvin *et al*, 1981). Training of teachers as counsellors was found to be effective in India (Kapur & Cariapa, 1980). The Child Youth and Development Centre in Manila has expanded its area of work by integrating mental health activities into school curricula (Yatco, 1979). Training guidelines for child mental health programmes based in primary care are available, such as the World Health Organization's manuals on child mental health and development (WHO, 1982) and the training package on the recognition and management of children with functional problems (WHO, 1987). Many countries have developed their own mental-health training packages for primary-care workers, although these deal primarily with problems of adult mental health.

Several developing countries are looking at ways of facilitating early child development through stimulation programmes linked with primary-care programmes for health and nutrition (Myers, 1988). Psychiatrists in SE Asia are developing strategies for health workers to be able to use psychotherapeutic skills to enhance coping skills and facilitate health compliance in risk groups of families (WHO, 1989).

The role of the child psychiatrist

It is clear, in the light of programme needs discussed, that the role of the child psychiatrist is not that of clinician alone but of planner, teacher and research worker. Acceptance of such a diverse role can cause problems, and conflicts arise when prioritising time. There may have to be a reduction in time spent on developing individual clinical interests. Liaison with other professionals is an important aspect of work for highlighting the value of child psychiatric approaches. The child psychiatrist may also have an important part to play in advocacy for change in social policy such as recognition of abusing situations like exploitative child labour, and provision of better institutional child care or day care for groups of children at risk.

Training in child psychiatry

The potential role of the child psychiatrist and the need for child psychiatric expertise at various levels of health care have implications for training at an undergraduate and postgraduate level. Most undergraduate schools have some psychiatric input though not always specific content with regard to child psychiatry. There may be a reluctance among the traditional specialties of medicine and surgery to give equal weighting to paediatric and psychiatric courses (Bartlett, 1989). There is also a tendency to emphasise issues relating to adult mental illness in psychiatric courses even in countries where children constitute between a third and a half of the population. Epidemiological data reviewed in this paper highlight the value of undergraduate training which is orientated towards the development of psychosocial skills and knowledge appropriate for use in community health settings.

Training in child psychiatry for clinicians working in developing countries is an issue of some importance. Child psychiatric work in the foreseeable future in most developing countries will be done not only by child psychiatrists but by paediatricians, general psychiatrists, and psychologists. Many countries have postgraduate training in psychiatry and paediatrics which may therefore require review and revision with regard to child psychiatric content. A recent symposium on postgraduate psychiatric training looked at the needs and constraints of psychiatric training in developing countries. An outline of training which included theoretical knowledge, and development of clinical, research, teaching and administrative skills required for work in child psychiatry was contained in the report of this symposium (Cox, 1989). A course for child psychiatry developed in Britain for overseas trainees is unfortunately not easily accessible to trainees because of current fee structures for overseas students. There is a place for regional initiatives with inputs from specialised centres in other countries, and this would be a useful form of collaboration between developed and developing countries. These efforts could take the form of regional study groups such as held recently for the development of leadership skills in the African region (Checkoway & Orley, 1990).

Research needs

Work in developing countries provides considerable scope for developing a clearer understanding of psychopathological processes, and also for development of innovative, feasible and cost-effective clinical strategies. The researcher in this context has to focus on issues of clinical relevance and is often constrained by a lack of resources. Many important areas requiring study have been identified in this article, including research into the way individual differences and socio-cultural factors interact to mediate experiences, or the impact of chronic malnutrition and anaemia on the cognitive processes of children. There is a need for culture-appropriate criteria to permit consistency in diagnosis (Olukoyade-Jegede & Olawatura, 1982). Work on the development of culture-appropriate indicators of development has commenced as a collaborative study co-ordinated by the World Health Organization (1986). The need for systematic evaluation of treatment approaches which are feasible for use in centres with limited resources or in primary-care settings has already been commented on.

Research methods suitable for use in developing countries must also be identified. Many of the studies reported in this paper have used screening procedures or interview techniques developed in a different country and culture. Techniques adopted from other settings need to be adapted to allow for differences in reporting due to situational, cultural or semantic factors. Teacher ratings were affected by classrooms being overcrowded in Hong Kong (Luk *et al*, 1988). A tendency towards over-rating by Hispanic mothers may have contributed to high rates observed in Puerto Rico (Bird *et al*, 1988). Misinterpretation of questions on eating habits appeared to result in misleading responses in a recent study of eating attitudes in Indian schoolgirls (King & Bhugra, 1989). Questions must also be formulated so as to take into consideration the characteristics of interviewer and informant. This was done for the Reporting Questionnaire for Children (Giel *et al*, 1981), leading to a few simple questions with a yes/no response since this format was considered likely to give accurate reporting within the context of the developing country being studied. Such a format contrasts with questionnaires and schedules used in developing countries. It is important to explore whether questionnaires or interview formats cover areas of concern for the target population.

Conclusion

Child psychiatry in developing countries is now an established field. These countries are subject to rapid socio-cultural and political changes which affect the life-styles of children and their families and hence their physical and emotional well-being. The need for child psychiatry is highlighted by established links between psychosocial factors and physical health, and existing morbidity among children due to mental health problems. Child psychiatric skills and expertise cannot therefore be restricted to sparse centres at a secondary or tertiary level. The specialist with child psychiatric skills may have to spend a substantial amount of time providing leadership and training for the development of community-based resources for child mental health. Academic work is also needed for the expansion of knowledge of psychopathology and for the development of effective and feasible clinical strategies. Child psychiatry can also contribute to changes in social policy about children. The diverse role of the child psychiatrist demands training which equips clinicians for these demands. The practice of child psychiatry in such a context can be exciting, challenging and of great relevance to the well-being of children as a whole.

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Lecture

Dangerous Mistakes

NIGEL WALKER

The shortening of the periods of detention for treatment, deterrence or retribution have made a live issue of whether (or when) it is justifiable to detain violent and sexual offenders solely for the protection of others. Anti-protectionist arguments have made 'dangerousness' a dirty word, but are based either on actuarial statistics of doubtful relevance or on confused moral reasoning. A typology of 'dangerousness' is tentatively offered, and the impossibility of adequately supervising some dangerous offenders in the community is emphasised. That said, offenders detained solely for the sake of others are entitled to more than merely 'humane containment'.

The best memorial to Henry Maudsley which I have read is by the late Peter Scott (1960). It records Maudsley's virtues without adulation and his shortcomings without condemnation. In some ways, Maudsley was rather backward looking: in a generation which was beginning to appreciate Darwin, he clung instead to Morel's notion of degeneracy – as of course did Lombroso, but Darwin's writings were more accessible to Maudsley. On the other hand, in a culture which was preoccupied with the crimes of the poor, Maudsley saw that 'white-collar' crime should be taken equally seriously – a point of view which did not gain real acceptance until well into the 20th century.

On the restraint of offenders in order to protect others, Maudsley took rather an extreme view. He was pessimistic about the effectiveness of attempts to treat adult recidivists, whether mentally disordered or not: he was in no way responsible for the excessive therapeutic optimism which later swept northern Europe and the United States. His pessimism led him to favour a sort of permanent segregation for chronic offenders, which is very much at odds with current attitudes.

Actuarial statistics

This paper is concerned with only two of the hazards of life: violence and sexual harm. They are not in the first rank so far as actuaries are concerned. They account for far fewer deaths, injuries and ruined lives than does the motor car, for instance. But attitudes to hazards are important: the notion of being attacked is much more worrying than the thought of falling victim to a road accident, or to some noxious feature of the environment. Actuaries may tell us that assaults are much less probable, but somehow this fails to reassure. Part of the reason must be that we think of attackers as selecting us as their targets, whereas accidents and other harms are unselective agents which we think we can usually dodge with a certain amount of care.

Actuarial estimates are used by governments to try to reassure citizens about crime. There is an important difference between actuarial and actual probabilities. No doubt the actuarial probability that city dwellers in a certain age group will be mugged in their lifetime is very small: but it is very much larger if they live in certain districts, and are in the habit of venturing out of doors at late hours. An individual's actual risk is not something that can be readily quanitified, but it is more real – and sometimes greater – than any actuarial statistic, which probably lies in no man's land.

The same point needs to be made in an inverted way about the individuals who are regarded as dangers because of what they have done, and who are in mental hospitals, in prisons, or under what is optimistically called 'supervision' in what is euphemistically called 'the community'. We are given statistics which are intended to reassure us about the likelihood that they will repeat the harm they have done. The motivation behind the statistics may be humanitarian or it may be economic. It does not, however, compel us to accept the statistics themselves entirely at their face value. Most of them are based on rather short follow-ups, which are long enough to answer such questions as 'Do men re-offend oftener than women?', but are not long enough to answer the question 'How many rapists ever re-offend?'. As Gibbens (1976) showed, a long follow-up is the only sound basis for an answer to that sort of question.

We may be told that adults suffering from mental disorder are no more likely to commit serious violence than other adults are; but this is another misleading actuarial statement. Even if it is accurate in a sense – and researchers seem to disagree about this – it

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This paper is based on the 1990 Maudsley Lecture.

is couched in terms of average probabilities. Now if the average were the mode – that is, the most frequently occurring value – it would be a meaningful statistic. But since mentally disordered people are diagnostically heterogeneous, the average almost certainly lies in a gap between diagnostic groups, some of them having probabilities lower than the average, others having higher probabilities, but few, if any, coinciding with the average. The same, of course, is true of people who are not mentally disordered, except that we use other ways of subdividing them into categories.

Nevertheless, let me play the actuarial game for a moment. In 1973 the Butler Committee were given the following findings by the Home Office (unpublished paper): 334 men who had been discharged from hospital orders in 1971 were followed up for two years, and their reconvictions were compared with those of nearly 3000 men who left prison in the same year after serving short sentences. The percentages convicted of violent or sexual offences within that short follow-up were as follows:

(a) ex-patients who had previously been convicted of violent or sexual offences: 17%
(b) ex-prisoners who had previously been convicted of violent or sexual offences: 22%

The figures are not reassuring, being much higher than those of other groups in the sample, which did not exceed 7%. If in order to be reconvicted of a violent or sexual offence within such a short follow-up the offender had to commit an offence, be identified, found, arrested, brought to court, and sometimes committed to a higher court for trial, these offenders must have been re-offending well within two years. If the follow-up had been five years, the percentages would have been higher still.

This reinforces what was said a long time ago by William Kvaraceus. "Nothing predicts behaviour like behaviour". This, however, is where another humanitarian, anti-protectionist argument begins. It points out that previous behaviour may be the most powerful predictor, but it is not powerful enough to be a reliable predictor. In criminological terms, less than 50% of men who have committed violent crimes will be proved to have committed further violent crimes. This is not a universal truth: my studies of three large samples have shown that if an offender has four or more convictions for violence the probability that he will acquire another is well over 50%. But men with four or more violent convictions are in a minority. So far as the rest are concerned the anti-protectionist premise has to be granted: their probability of re-offending is less than 50%. So, the argument goes, a policy which detains them in order to protect others makes more mistakes than a policy which releases them as soon as the law allows.

Anti-protectionism

The fallacy – I call it the 'arithmetical fallacy' to distinguish it from the actuarial fallacy – is obvious. The argument counts only mistakes, giving equal weight to one which involves mistaken detention and one that leads to an avoidable casualty. Both kinds are regrettable, but regrettability is all they have in common, and any attempt to weigh them on the same scales is wrong-headed.

The Swedish Council for Crime Prevention (1978), however, has offered an anti-protectionist argument that goes further still, and would apply even to situations in which a policy of detention would involve fewer mistakes than a policy of release. To detain someone simply for the protection of others, they argued, is to punish him for a crime he has not committed and may never commit. The rhetoric is more impressive than the reasoning. The key word in the argument is 'punishment', with its retributive connotation. It assumes that every sort of detention must be punitive, and it implies that you should never restrain or even inconvenience anyone for fear of what he might do if there is the slightest chance that he will not do it. For example, a man who has assaulted his wife should not be ordered to stay away from her in case he does so again, because that would be punishing him for what he may not do. It implies that any order of a court must be regarded as retributive punishment, and judged accordingly: even a hospital order.

A similar, but more sophisticated, argument was put forward at the Broadmoor Symposium on dangerousness convened by the late John Hamilton in the early 1980s. Since it seems to avoid the notions of desert and punishment, it must be seriously considered. It invites us to compare our attitudes to two imaginary groups. For the sake of simplicity, both groups consist of three men, and in both cases we have good actuarial reasons for believing that one of each trio will commit serious violence if free to do so, but no means of knowing which of the three it will be. One of the groups consists of men convicted of violence, but none of the other trio have been convicted. The awkward question is why we should feel justified in detaining the convicted trio for a long period solely for the protection of others when we would not feel justified in so detaining the unconvicted trio.

The soundest answer was provided by the Floud Committee on Dangerousness and Criminal Justice (1981). The vast majority of citizens in our society do not commit serious harm, and are regarded as having a right to what can be called "the presumption of harmlessness". From time to time, people who are presumed harmless turn out not to be, but until they do there is not much we have the right to do about them, apart from taking sensible precautions that do not involve interfering with them. For both practical and moral reasons we have to put up with what can be called "the general risk of harm". But when a person has been proved to have inflicted serious harm on someone else, the presumption of harmlessness no longer applies, and we are entitled to make him a target of our precautions. This does not oblige us to lock him up if the risk he seems to represent is negligible; but it does give us the right to do so if it seems more than negligible. Nor is it a question of what he deserves: his mental state may be such that what he did is totally excusable, but our precautions are not meant to give him his deserts.

I have cited these anti-protectionist arguments in order to emphasise their popularity in the 1970s and 1980s. What brought them to the surface was the shortening of sentences and the shortening of the periods considered necessary for the treatment of most mental illnesses. In an era in which offenders were detained for long periods because it seemed necessary to deter, to treat, or to give them what they deserved, the question of whether the protection of others was a proper reason was rather academic, except where a few lifers and some 'special hospital' patients were concerned. Even while judges were shortening determinate sentences it was noticeable that they hardly ever used the special extended sentences which the law expressly allowed when an offender's record indicated that the public needed protection from him. Occasionally a life sentence would be used rather than the normal determinate sentence, if psychiatrists said that the offender was mentally unstable; but that was rare, and sometimes overturned on appeal. Meanwhile psychiatrists were more frequently discharging the mentally ill after quite short stays in hospital. The result was that precautionary detention became a live issue, and academic anti-protectionists found receptive audiences.

The other operative factor was the misinterpretation of follow-ups. I have already pointed out that most of them were far too short, but even long follow-ups had concealed pitfalls. A commonplace observation was that very few people who had committed homicide did it again. This is true, but the proper scientific question was "What percentage of people who commit violent offences that were or might have been fatal later committed violent offences that were or might have been fatal?". I have never seen an attempt to answer this question, but it might well be a much larger percentage.

The result was that 'dangerousness' became a dirty word. I can even detect the deliberate avoidance of the word in one of the Royal College of Psychiatrists' documents, the 1989 *Guidelines for Good Medical Practice in Discharge and After-Care Procedures*. I have no criticism of what the *Guidelines* actually recommend: I merely notice that patients who would in earlier decades have been referred to as 'dangerous' are now concealed in the category 'vulnerable' patients.

Psychiatric reluctance to call a patient 'dangerous' can be traced at least as far back as the late Peter Scott, who may well have been the first to remark that 'dangerous' is a dangerous label. He used to emphasise that many patients are risks to others only if they find themselves in certain situations – for example heated quarrels – or certain conditions such as after prolonged drinking. He was, however, wise enough not to claim this is true of all patients.

A tentative typology

We need a 'typology of dangerousness'. It might perhaps comprise four types. The first type is the individual who harms others only if sheer bad luck brings him/her into a situation of provocation or sexual temptation. One might make distinctions here, according to the degree of provocation or temptation which is sufficient. The second type is the individual who gets into such situations not by chance but by following inclinations. Examples are men who, having killed or seriously injured women with whom they have been cohabiting, seek similar relationships after they have been discharged, or child molesters who find jobs as school caretakers or in youth clubs. We are more competent than we were at preventing child molesters from finding jobs of this kind, but supervisors still find it very difficult to control supervisees who repeatedly enter into close emotional relationships with adults, as my experience on the Parole Board confirms.

These first two types can fairly be called only 'conditionally dangerous'. The third, however, consists of individuals who are consciously on the look-out for opportunities. One might call them 'opportunity-seekers'. The fourth type is the 'opportunity-maker', who does more than look for his opportunities. I am not suggesting that there is a sharp distinction between these two kinds of behaviour; a frustrated opportunity-seeker might decide to make an opportunity, or vice versa. My point is that individuals who behave in these ways cannot be dismissed as merely conditionally dangerous. They are unconditionally dangerous. And in case anyone thinks that opportunity-makers are members of a rare minority, let me quote from Wyre (1986), who has specialised in the treatment of sexual offenders:

> "Sexual attacks seem spontaneous but most have been planned at least in some respects. . . . Often the attacker has had previous experience. Even before an attack is

> consciously planned it is slowly formulated in the flawed sexual imagination of the assailant. . . ."

There can be no list of signs or symptoms which will assign patients or prisoners to one of these types, but I can offer two thoughts. One is Kvaraceus' slogan: "Nothing predicts behaviour like behaviour"; and he meant the behaviour of the individual, not of an actuarial group. In more precise terms, actuarial information about the behaviour of a group to which the individual can be assigned by virtue of relevant variables is likely to have less predictive power than information about the individual's own past conduct. My second offering is a quotation from Maudsley himself (1888):

> "What is required now is full and exact investigation and faithful record of cases . . . by painstaking and searching inquiries into their hereditary antecedents, their mental and bodily characters, the conditions of their training, and the exact circumstances of their crimes. . . ."

You may think it presumptuous to emphasise the importance of history-taking, but there are points which need to be made about history-taking in criminal cases. For example, the information about what Maudsley called "the exact circumstances of crimes" is not always available from reports of the trial. I recall one case in which all that the clerk of a magistrates' court told the psychiatrist was that the accused had "taken a knife to frighten his wife", when in fact he had tried to stab her with it. The wife's account would have been more informative. (The patient was soon allowed day leave, went home and killed her.) Witnesses often are not allowed to say all they know at a trial, and social inquiry reports are often influenced more by what the offender says than by what others say about him. The same is true of previous relevant behaviour. Official information about previous offences often takes the form of the police record: "assault, one year's imprisonment, suspended for two years", or "indecent assault: two years' probation". These may well understate the actual offence or attempted offence, because the prosecution could not, or chose not to, support a more serious charge, such as attempted murder or attempted rape. The result is sometimes called 'undercharging', and it means that taking convictions involving violence or sex at face value may seriously underestimate dangerousness.

Undercharging may explain something that I have noticed in the case of indecent exposers. By tracing the careers of a large sample of hospital-order cases in the 1960s backwards and forwards, through police records, Mrs McCabe and I found that not all indecent exposers were the harmless specialists they are so often said to be (Walker & McCabe, 1973): nearly half had convictions for other sexual offences. On comparing our finding with those of other researchers we realised that they were much the same. Bluglass' (1980) study of a West Midlands sample suggests that it is the aggressive exposers who are the most likely to progress to more serious offences. It seems that indecent exposers benefit from the "presumption of harmlessness' to an extent that is by no means always justifiable.

There is only one more point to make about previous behaviour, and it is almost too obvious to make. Previous convictions may not – often do not – draw attention to all that an offender has done. This is almost as true of violent or sexual offences as it is of shoplifting or bad driving. In the first place, our acquittal rates are rather high. Gibbens (1976) found that acquitted rapists often acquired subsequent convictions for rape. Unfortunately – at least for psychiatric purposes – the official police records do not include acquittals. Nor do they include incidents which, for one reason or another, never reached a criminal court. The offender himself could tell you about them, but probably will not.

Yet suppose that you are convinced that the prisoner or patient really has done nothing similar before. There may still be reason for concern lest the offending should be repeated in the future. From Parole Board experience, I can mention some of the indications for repetition. An obvious example is the case in which the violence was committed after heavy drinking. The offender may well be only 'conditionally dangerous', but when he is discharged it will be very difficult to be sure that he will not drift back into heavy drinking. Supervision in the community may be of use in such cases, and is covered later in this paper.

Weapon-carrying is a more complex matter. Obviously a man who has stabbed someone and is found to have been an habitual knife-carrier is at least 'conditionally dangerous'. But when a young man from what is euphemistically called 'an inner-city background' says that he carries a knife simply for his own protection, and is not suspected of being a member of a street gang, I am inclined to believe him. It may mean that if driven to defend himself or his girlfriend he will inflict serious injury, but it does not necessarily mean that he will initiate violence. I am more worried by men who own firearms (or crossbows) for psychological rather than practical reasons. They may be members of rifle or pistol clubs: but that is not reassuring. I would particularly want to know whether they have unofficial stocks of ammunition at home.

More interesting, perhaps, are indications with which clinicians are familiar. Obvious examples are jealous or persecutory delusions. Taylor (1985), whose studies of schizophrenic violence are well known, states that she would also list 'delusions of passivity'. If I, a non-clinician, might venture an addition, it would be 'delusions of provocation'. For example, a man who has attacked a stranger sometimes gives the somewhat abnormal explanation that "he was staring at me". It is not always easy to ascertain whether in fact the stranger was deliberately doing this or whether the assailant is pathologically sensitive. Either way, a man who responds with violence to being stared at cannot be presumed harmless.

Patients and prisoners sometimes offer justifications for what they have done. Their justifications are often merely attempts, after their crime, to restore their self-respect, or the respect of others. Paedophiles, for example, often claim that their victims made the first approaches. Whether the offender felt justified when he committed his crime, or merely succeeded in justifying it later, I suggest that he may be more likely to re-offend than one who does not justify it. I am not talking about obviously deluded justifications like orders from God or the Devil, but simply about a conviction that what one has done was right.

More than one contributor to Hamilton's Broadmoor Symposium (1982) expressed special concern about men who are arrogantly sure of the rightness of whatever they do. Most worrying is the offender who seems unable to empathise with his victims, regarding them simply as instruments or obstacles. One can observe this attitude not only in some mentally disordered patients, but also in some prisoners, and even in some law-abiding citizens whom we merely call ambitious or single-minded; but when it is observed in a violent or sexual offender it must be a ground for extra concern.

What I have been leading up to is a general point about predicting further harmful behaviour. If anyone still hopes that follow-up studies will tell us by how much the presence of a certain indicator increases the risk, I can safely say that it will be a long time before that is achieved. It could be achieved only by large samples, painstaking interviews of both offenders and other people involved, and lengthy follow-ups. The most that can be expected from small-scale research is the occasional negative finding, for example, that something which has been regarded as a predictor is in fact not, or at least not in some types of case. This might save some offender-patients from being detained for as long as they would otherwise.

Yet even if large-scale, meticulous research did succeed in identifying more predictors, this would have its dangers. There would be a tendency to assume that every predictor, when present, increases the risk. Yet predictors may overlap. Very careful analysis is needed to establish whether predictor X adds to the predictive power of predictor Y. It will be a long time before we can do without clinical 'hunch' and individual history.

A special point needs to be made about the offender whose hate or sexual interest seems to be focused on a particular victim, or on a person who takes the place of a former victim. The following case history illustrates more than one point.

> S was a man whose first wife divorced him because of his violence. He soon married again, and strangled his second wife. Having served ten years of a life sentence for this crime, he was released on licence. After settling down to run a small business he married a third time. His third wife soon left him to live with her mother, unfortunately not far enough away. One night he was found prowling round their home with an air-pistol. When he was brought to court for this the judge said that he was reluctant to send him back to prison because he had already spent so many years there. The supervising probation officer clearly doubted his ability to control S if he were to be left at liberty, but the judge said that it was a risk he was prepared to take. The wife was not asked if it was a risk she was prepared to take. Within a few weeks S had broken into her home, and shot her, her sister and himself with a firearm. At no time were prison doctors able to give him a psychiatric label, yet clearly he was a dangerously abnormal individual, whose abnormality manifested itself only in his marital relationships.

The most important question which this story raised was "Who has the right to say 'It's a risk I am prepared to take?'".

Another point which this anecdote illustrates, although perhaps in a rather extreme way, is the difficulty of supervision in the community. There are cases in which reoffending is preceded by a gradual deterioration in the offender's condition or behaviour, for example as a result of repeated heavy drinking, failure to take prescribed drugs, or even failure to keep appointments. In such cases an alert supervisor can, with no more than a telephone call, recommend swift intervention. Sometimes an offender's family or hostel can be enlisted by the supervisor, and will report signs which call for action. Women who are entering into long-term relationships with wife-attackers can and should, be told their histories, if necessary by the supervisor. But supervision can never amount to surveillance; and the offenders whom I have called 'opportunity-makers' or 'opportunity-seekers' are safe only under a degree of surveillance which it is hardly possible to provide. It might be better if the term 'supervision', which gives an exaggerated impression of effectiveness, were abandoned in favour of some word such as 'monitoring'. A 'monitor' is merely a person who warns *when he notices.*

Even monitoring a dangerous ex-inmate raises delicate ethical problems. The monitor himself must, of course, be given all the relevant information about the ex-inmate's history; but how much should be passed on to an employer, a hostel warden, a landlady, or a cohabitee? The more the monitor can induce the ex-inmate to tell him about his present way of life and problems, the better. But the more the man confides in him the more qualms he may have in using this information to recommend recalling him to hospital or prison. My two tentative suggestions are these. The relationship between a professional carer and someone who has been given into his charge by law, and for the protection of others, is not a voluntary relationship, and so does not carry the same moral obligations or constraints. The compulsory patient's or ex-patient's interests should not over-ride the interests of others. My second point is that if any professional carer feels that he cannot make this distinction, he should refuse the responsibility. This sounds uncompromising; but I do not see how a compromise could be truly ethical.

Conclusions

I am not trying to put the clock back: simply suggesting that there are people who have made it go a little fast. Their arguments are partly actuarial, partly moral: but neither sort stands up to close examination. We do not have, and are not likely to have in the foreseeable future, prediction tables that will tell us who can be released with little risk to others. Nor can we assume that any substantial risk will be greatly reduced by supervision in the community. Clinical judgement must continue to be the basis for recommendations.

At the same time, the detained offender is entitled to consideration. If he has reached a stage at which treatment no longer offers hope of rendering him harmless, if it can no longer be argued that he deserves further deprivation of liberty, in short if the protection of others is the sole reason for not releasing him, then in a sense he deserves something by way of compensation for being sacrificed to the interests of others. That compensation, I suggest, must lie in the quality of his life inside. In plain terms, what I am suggesting is that we have a moral duty to make the conditions of incarceration as tolerable as possible. There is an official phrase, 'humane containment', which is sometimes used by the Prison Service. But it seems to me that while 'humane containment' may be all that we owe, or can give, to people serving determinate sentences, what we owe to people who are being detained for the sake of others is something better. The Council of Europe's (1983) recommendation is "a pleasant environment", which sets a higher standard. Admittedly it is a standard which few secure institutions in Britain can claim to attain; and shortage of resources may make attainment a long-term goal. But it should be the goal: 'humane containment' is not quite good enough.

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Unexplained Fluctuations in the Risk for Schizophrenia by Month and Year of Birth

R. E. KENDELL and W. ADAMS

Variation in their year and month of birth was studied in the 13 661 schizophrenics born between 1914 and 1960 known to the Scottish Psychiatric Case Register. Year-to-year fluctuations in the number of schizophrenics per 10 000 live births were outside chance limits. So were month-to-month fluctuations between January 1932 and December 1960, and this was largely due to fluctuations in the numbers of schizophrenics born in February, March, April and May. Time-lagged correlations with mean monthly temperatures suggest that in these same four months the incidence of schizophrenia is influenced by temperature six months previously – the lower the temperature in the autumn the higher the incidence of schizophrenic births the following spring. If these findings can be confirmed in other data sets, they would suggest that some influence which varies consistently with season and temperature is contributing to the aetiology of schizophrenia and may exert its effects as early as the third or fourth month of foetal development.

It is well established that, throughout the temperate latitudes of the northern hemisphere, schizophrenics are born in the winter months more frequently than other people (Bradbury & Miller, 1985). Although the pattern varies somewhat from year to year and place to place there is generally an excess of schizophrenic births of about 8% in January, February and March. As the birth dates of the siblings of schizophrenics do not appear to differ from those of the general population (Buck & Simpson, 1978) this excess of winter births suggests that some seasonally varying influence is contributing to the aetiology of schizophrenia, either *in utero* or possibly in the early months of life. An intra-uterine viral infection is perhaps the most plausible of many possible explanations of this 'season-of-birth' effect, partly because of the accumulating epidemiological and neuropathological evidence that damage to the foetal brain at or before the time of birth may contribute to the genesis of schizophrenia.

An attempt by Kendell & Kemp (1989) to find out whether the birth cohorts who were *in utero* during the 1918/19 and 1957 epidemics of influenza A were subsequently at increased risk of schizophrenia involved examining the dates of birth of all patients admitted to hospital in Scotland since 1963 with a diagnosis of schizophrenia. Although there was no evidence of such an increase, it was apparent from these data that there were substantial fluctuations in the numbers of schizophrenics born in different months and years. This paper describes the investigation of these fluctuations and attempts to relate them to variations in temperature.

Method

Since 1 January 1963, the Scottish Health Service has collected standardised information (known as SMR4 data) on all admissions to and discharges from all psychiatric hospitals and in-patient units in Scotland. All admissions and discharges with an ICD–9 diagnosis of schizophrenia (World Health Organization, 1978) were extracted from this national register and the successive admissions and discharges of individual patients linked together using surname, sex, date of birth and hospital case reference number. In an attempt to restrict the study to 'genuine' schizophrenics, all patients who did not have either a current admission diagnosis of schizophrenia (most of these were long-term in-patients) or at least two previous discharge diagnoses of schizophrenia were excluded. After excluding patients whose exact date of birth was unknown, this left a population of 13 661 schizophrenics born between 1 January 1914 and 31 December 1960.

Results

The number of schizophrenics per 10 000 live births was calculated year by year (Table 1, Fig. 1). The number rises steadily from 1914 to 1925 and falls fairly steadily from 1948 to 1960. This is largely because the register was only created in 1963 and the data extracted from it in 1989. Patients born early in the century would either have died, or at least ceased being admitted to psychiatric hospitals, before 1963; and those born in the 1950s would not yet have passed through the whole of the risk period for developing the illness. What is important is not the overall shape of the distribution but the sharp year-to-year fluctuations. Why, for example, were so many schizophrenics born in 1938 and 1945 and so few in 1935 and 1947? This was the phenomenon that aroused our interest.

Table 1
Numbers of known schizophrenics per 10 000 live births in Scotland, 1914–60

Year of birth	No. of schizophrenics	No. of live births	Schizophrenics per 10 000 live births
1914	197	123 934	15.90
1915	203	114 181	17.78
1916	207	109 942	18.83
1917	185	97 441	18.99
1918	216	98 554	21.92
1919	253	106 268	23.81
1920	332	136 546	24.31
1921	349	123 201	28.33
1922	347	115 085	30.15
1923	324	111 902	28.95
1924	319	106 900	29.84
1925	375	104 137	36.01
1926	351	102 449	34.26
1927	329	96 672	34.03
1928	351	96 822	36.25
1929	363	92 880	39.08
1930	354	94 549	37.44
1931	377	92 220	40.88
1932	353	91 000	38.79
1933	320	86 546	36.97
1934	341	88 836	38.39
1935	264	87 928	30.02
1936	316	88 928	35.53
1937	321	87 810	36.56
1938	370	88 627	41.75
1939	322	86 913	37.05
1940	298	86 392	34.49
1941	277	89 748	30.86
1942	291	90 703	32.08
1943	298	94 669	31.48
1944	327	95 920	34.09
1945	347	86 924	39.92
1946	355	104 413	34.00
1947	324	113 147	28.64
1948	354	100 344	35.28
1949	324	95 674	33.86
1950	260	92 530	28.10
1951	284	90 639	31.33
1952	279	90 422	30.86
1953	266	90 913	29.26
1954	212	92 315	22.96
1955	215	92 539	23.23
1956	227	95 313	23.82
1957	188	97 977	19.19
1958	158	99 481	15.88
1959	190	99 251	19.14
1960	148	101 292	14.61

Year-to-year variation

There is no reason why the distribution of numbers of known schizophrenics per 10 000 live births (for simplicity, the 'incidence' of schizophrenia) should conform to any particular pattern between 1914 and 1960, either year by year or month by month. There are good reasons why the 'incidence' rises between 1914 and 1925 and falls between 1950 and 1960; but there is no reason why the overall shape should take any particular algebraic form. On the other hand, the curve should be smooth, with no changes from year to year or month to month beyond chance expectation.

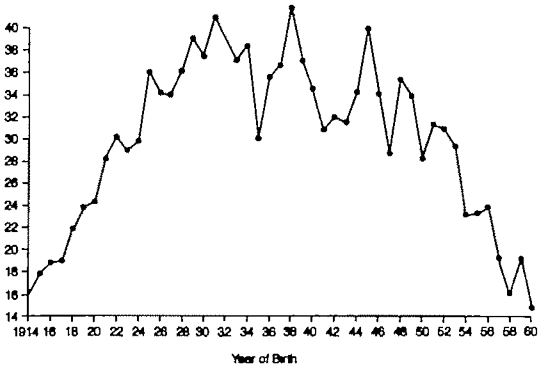

Fig. 1 Known Scottish schizophrenics per 10 000 live births.

If a set of consecutive rates – in this case the 'incidence' of schizophrenia in the 47 consecutive years from 1914 to 1960 – is homogeneous, the rates in successive time periods (t) will conform to a Poisson distribution. In algebraic terms:

$$P[R_t = r_t] = \frac{(\lambda_t N_t)^{r_t}\, e^{-\lambda_t N_t}}{r_t!}$$

where λ_t = 'incidence' of schizophrenia at time t
N_t = total live births at time t
R_t = the number of known schizophrenics born at time t.

If, on the other hand, the set of rates is not homogeneous, the rates of successive time periods will only conform to a more general model. One such alternative to the Poisson distribution is the negative binomial distribution. In algebraic terms:

$$P[R_t = r_t] = \frac{\Gamma(r_t + {}^1/_c)}{r_t\, \Gamma({}^1/_c)} \left(\frac{c\lambda_t N_t}{1 + c\lambda_t N_t}\right)^{r_t} \left(\frac{1}{l + c\lambda_t N_t}\right)^{1/c}$$

The additional parameter c can be described as a variance inflation factor, and when $c = 0$ the negative binomial distribution is identical to a Poisson distribution. Variation beyond the limits of a Poisson distribution can therefore be identified by estimating c using maximum-likelihood methods and testing whether c is significantly greater than zero.

The log of the annual 'incidence' of schizophrenia (log λ_t) was plotted against t over the 47 years and the resulting curve fitted to a series of polynomials in t using weighted least squares. A quadratic in t produced a reasonable fit, that is, cubic and higher terms were not significant. Hence:

$$\log t = a_0 + a_1 t + a_2 t^2$$

where a_0, a_1 and a_2 are constants.

When the data were fitted to a negative binomial distribution the variance inflation factor (c) was significantly

Table 2
Years in which the 'incidence' of schizophrenia varied most from the Poisson distribution of the fitted curve

Year	Direction of deviation	P
1935	Low	0.0000
1941	Low	0.0007
1925	High	0.0032
1945	High	0.0036
1943	Low	0.0078
1952	High	0.0083
1942	Low	0.0089
1947	Low	0.0095
1953	High	0.0116
1958	Low	0.0116

greater than zero, implying that the rates do not fit a Poisson distribution ($c=0.0059$; 95% confidence limits 0.0028–0.0105).

This evidence that year-to-year variation was outside chance limits was confirmed by a test for overdispersion derived by the method of Cox (1983), for which the dispersion statistic had a value of 7.19 and $P<0.01$.

The ten years for which the 'incidence' of schizophrenia varied most from the quadratic fitted curve are listed in Table 2. The two most aberrant years in this 47-year series are 1935 and 1941, in both of which the 'incidence' of schizophrenia was abnormally low. The years with the most conspicuously high 'incidence' were 1925 and 1945.

Month-to-month variation

Because records of the numbers of live births per month in Scotland are no longer available for before 1932, month-to-month variation in 'incidence' could only be studied in the 8229 schizophrenics born in the 29 years from 1932 to 1960. The statistical procedures used were the same as those described above and this time the set of consecutive rates consisted of the 'incidence' of schizophrenia for the 348 months from January 1932 to December 1960. As before, the log of the monthly 'incidence' of schizophrenia ($\log \lambda_t$) was fitted to a series of polynomials in t using weighted least squares and the best fit was provided by a quadratic equation, i.e. cubic and higher terms were again not significant.

The data were therefore fitted to a Poisson distribution of this quadratic. Estimation of the residuals averaged over each month revealed that positive values occurred only in the four consecutive months February–May (Table 3). Separate analyses were therefore carried out for these four months and the other eight (June–January). When these two data sets were fitted to a negative binomial distribution the variance inflation factor c was significant ($c=0.018$; 95% confidence limits 0.005–0.034) for the February–May data, but not for the June–January data ($c=0.006$), implying that the latter do have a Poisson distribution whereas the former do not. This was confirmed by the dispersion statistic which had a value of 3.77 ($P<0.01$) for February–May but only 1.24 ($P>0.05$) for June–January. Furthermore, the difference in $\log \lambda_t$ for these separate monthly sequences was constant from 1932 to 1960; that is, the two curves were parallel, implying that the rate of change from year to year in the 'incidence' of schizophrenia is the same in the February–May and June–January populations.

The presence of an excessive number of large residuals in a regression can be detected by a half normal plot. This is a plot of the absolute standardised residuals against their expected values. The term 'standardised' indicates the value divided by its standard error, and when absolute values are used this means the distribution is half normal. When the data conform to the model the plotted values lie in a straight line; but if there is significant overdispersion the points drift above the line as the residuals increase. As Fig. 2 shows, the residuals for February–May, but not those for June–January, do indeed drift above the line, indicating that year-to-year variation in the 'incidence' of schizophrenia is excessive in these months, and that this is not attributable to the familiar higher incidence at this time of year shown in Table 3.

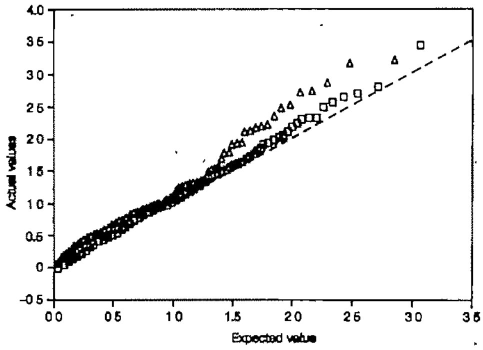

Fig. 2 Half normal plots of standardised residuals (△ February–May, □ June–January).

Table 3
Monthly indices over the 29-year period 1932–60

January	February	March	April	May	June	July	August	September	October	November	December
Mean values of residuals (actual minus fitted) when all data are fitted to a line $\log \lambda_t = a_0 + a_1 t + a_2 t$											
−0.20	2.44	1.92	1.04	3.07	−1.63	−1.45	−1.64	−0.87	−1.45	−0.15	−1.08
Mean monthly 'incidence' of schizophrenia (cases per 10 000 live births)											
30.5	34.1	33.2	32.0	34.2	28.3	28.6	28.3	29.2	28.4	30.1	28.9

Relationship between incidence and mean monthly temperature

Viral infection, either of the foetus *in utero* or of the new-born infant, provides a possible explanation both of the raised 'incidence' of schizophrenia in February–May relative to the other eight months in the year and of the greater year-to-year variation in 'incidence' in February–May. As many viral infections have a characteristic seasonal distribution, and their incidence varies fairly predictably with changes in temperature and other climatic variables, an attempt was made to relate the observed month-to-month variation in the 'incidence' of schizophrenia to variations in mean monthly temperatures. Mean maximum, minimum and average monthly temperatures in Scotland (derived from daily recordings of maximum and minimum air temperatures in the previous 24 hours at 7–11 urban sites) were obtained from the annual reports of the Registrar General for Scotland for the years 1931–61; that is, for a 31-year period starting 12 months before and ending 12 months after the 29-year period for which the monthly 'incidence' of schizophrenia was known.

Mean monthly temperatures obviously vary with the season of the year. However, we examined the difference between the mean temperature in any particular month and the overall mean temperature for that month between 1931 and 1961. As the fitted regression curves for the monthly 'incidence' of schizophrenia described above are derived from 29 years' data (1932–60) they can be assumed to be adjusted to customary Scottish temperatures. Any correlation between the 'incidence' of schizophrenia and deviations in mean temperature from the average for that month must therefore be a function of temperature rather than of the season of year.

Efficient score tests (Cox & Hinkley, 1974) measuring the covariance between the residuals calculated previously for the monthly 'incidence' of schizophrenia between January 1932 and December 1960 and mean monthly temperatures between January 1931 and December 1961 were calculated and time lagged at monthly intervals from −10 months to +3 months. The results are shown in Table 4. (These score tests are derived from the average daily temperatures each month; corresponding calculations were also performed using mean maximum and mean minimum temperatures, and the results were very similar.) Efficient score tests measure the covariance between an existing set of residuals and an additional variable, and are a means of determining whether that additional variable – in this case deviations from normal temperature – significantly improves the regression curve. They can be assumed to have an approximately normal distribution: i.e. values greater than ±2 are significant, the sign indicating the direction of the correlation.

It can be seen from Table 4 that there are many individual months in which there is significant covariance between the 'incidence' of schizophrenia and temperature. However, there is no consistent trend except with a time lag of −6, that is, when the residuals for the 'incidence' of schizophrenia are matched against deviations from the mean monthly temperature six months earlier, in the third month of pregnancy. From February–June all values are negative, and significantly so in March, April and May. From July–January all values are positive. When these lagged temperatures were fitted as additional variables to the 'incidence' curves significant regression coefficients were obtained. From these it was calculated that, in February–May, for every degree drop in temperature below the overall mean six months before (i.e. August–November) the 'incidence' of schizophrenia increases by over 7% and falls by 7% for every degree rise in temperature (4% for 1° Fahrenheit). In June–January, on the other hand, every degree Celsius drop in temperature below the overall mean six months before is associated with a decrease in 'incidence' of just 1.8%, and a corresponding rise in 'incidence' for every degree rise in temperature (1% for 1° F).

Table 4
Time-lagged efficient score tests measuring the covariance between existing residuals to the monthly 'incidence' of schizophrenia and mean monthly temperatures, 1931–61

	Month of birth											
Time lag: months	January	February	March	April	May	June	July	August	September	October	November	December
−10	−1.39	−1.45	1.27	−0.22	1.35	0.24	−2.80	0.19	0.44	−1.20	0.21	3.02
−9	−0.79	−1.49	0.29	−0.45	2.05	1.90	−0.75	−0.91	−0.82	0.86	0.94	1.40
−8	−3.43	−2.90	−0.96	1.41	−0.70	2.38	−1.39	−2.08	0.81	0.56	0.81	−0.27
−7	−2.07	−1.47	0.19	0.73	−0.40	2.43	−0.34	−0.12	3.11	1.27	1.34	−1.14
−6	1.21	−1.01	−2.93	−2.08	−2.32	−0.82	1.13	0.78	1.97	0.71	0.94	1.07
−5	−0.35	−0.38	−0.62	−0.09	−1.23	−0.41	1.08	1.01	−0.48	2.32	−0.18	1.44
−4	0.07	−0.52	−1.07	−2.55	0.92	−1.31	0.03	−0.19	0.80	−0.75	0.79	−0.30
−3	−1.09	0.44	0.01	0.33	3.59	−1.40	0.27	−0.67	0.62	−1.38	−0.27	0.47
−2	−0.66	0.61	0.62	0.17	2.76	−0.55	−0.05	−2.13	−0.16	−0.81	0.27	0.91
−1	−0.27	−0.32	3.39	1.70	0.34	1.38	−2.14	2.09	−0.83	−1.23	0.90	1.07
0	0.43	0.17	1.24	−1.56	0.32	−1.02	0.72	−0.90	0.06	−0.38	0.84	0.71
+1	−1.29	0.35	0.10	−0.03	0.75	−1.20	−0.66	0.97	−0.62	0.71	0.76	−0.18
+2	0.59	1.19	−1.47	−0.23	1.43	−0.64	1.99	−0.82	1.61	−0.06	1.19	0.84
+3	0.61	1.84	0.16	−1.03	0.30	−1.65	0.89	0.40	−0.48	0.46	0.32	−0.50

After including the six-month lagged temperatures in the regression, the new residuals were examined and a further set of score tests calculated to find out whether other temperature effects existed. None was found. As the variance inflation factor (*c*) in the negative binomial equation was reduced from 0.018 to 0.011 when temperature was included it seems that temperature variations contribute to, but do not entirely account for, the monthly fluctuations in the 'incidence' of schizophrenia in February–May.

Discussion

The central finding of this study is that there are unexplained deviations from the expected distribution of the years and months of birth of Scottish schizophrenics. Between 1914 and 1960 fluctuations in the annual number of known schizophrenics per 10 000 live births are outside chance limits. There are fewer than expected with birth dates in 1935, 1941, 1942, 1943, 1947 and 1958 and more than expected with birth dates in 1925, 1945, 1952 and 1953. Between January 1932 and December 1960, month-to-month fluctuations in the number of schizophrenics per 10 000 live births are also outside chance limits, and this is almost entirely due to fluctuations in the numbers of schizophrenics born in the four consecutive months of February–May. It is not simply that more schizophrenics are born in these months; the variation from year to year is greater in these four months than in the other eight. Moreover, time-lagged efficient score tests measuring the covariance between deviations from mean monthly temperature and deviations from the expected monthly 'incidence' of schizophrenia suggest that in these same months, March–May or February–June, the incidence of schizophrenia is influenced by temperature; the lower the average temperature six months before (i.e. in September–November the previous year) the higher the incidence of schizophrenia in March, April and May, and vice versa.

This could all be due to the chance effects of a variety of other influences liable to fluctuate over time, such as mortality rates, patterns of emigration and diagnostic criteria. Although the number of schizophrenics studied was substantial – a total of 13 661 and an average of 291 per year between 1914 and 1960 and 24 per month between 1932 and 1960 – this represents less than half the theoretical expected number. As Table 1 shows, the number of schizophrenics per 10 000 live births is rarely greater than 40. If the lifetime risk of schizophrenia is assumed to be about 1%, this figure should be close to 100. Many things contribute to the gap between these two figures. Infant and childhood mortality was still high in the 1920s and 1930s, and many young men died in World War II. In addition, a stringent definition of schizophrenia was employed. If patients with a single discharge diagnosis of schizophrenia had been included the total number of subjects would have been substantially higher, but many of these additional patients would not have been suffering from genuine schizophrenic illnesses. The study design also made it inevitable that schizophrenics who were never admitted to hospital, or migrated to other parts of the UK, or did not receive in-patient care in Scotland between 1963 and 1989 for other reasons, would have been missed. Some patients would also have been born outside Scotland. There has, however, been little immigration in Scotland in the last 50 years. The majority of immigrants were born in England or Ireland and are unlikely to constitute more than 20% of the patient population. None of these influences, however, singly or in combination, is likely to generate sharp differences in the number of known schizophrenics born in successive months or successive years. Even so, replication in a second data set is needed. It also needs to be established whether the findings are specific to schizophrenia.

Most previous studies of the dates of birth of schizophrenics have been concerned either with the excess of schizophrenic births in winter and spring or with possible relationships between the incidence of schizophrenia and the incidence of infections of various kinds in the general population. Watson *et al* (1984) and Torrey *et al* (1988) both compared the birth patterns of series of American schizophrenics with reported infections of various kinds in the general population. The former, in Minnesota, found significant correlations with the reported incidence of diphtheria, pneumonia and influenza. The latter, using data from Connecticut and Massachusetts, found correlations with measles, varicella zoster and poliomyelitis. Both, however, employed a series of different time lags and neither was testing an *a priori* hypothesis. Mednick *et al* (1988) did have a specific hypothesis, namely that the 1957 epidemic of A2 influenza in Helsinki was associated with an increased risk of schizophrenia in the children of women exposed to infection in mid-pregnancy. Their findings could not be confirmed either in Scotland (Kendell & Kemp, 1989) or reportedly in the USA but a relationship has since been reported between the monthly incidence of influenza and schizophrenic births in Denmark between 1911 and 1960 (Barr *et al*, 1990). It has also been claimed that there are unexplained fluctuations in the year of birth of patients with idiopathic Parkinson's disease and that these too can be related to epidemics of influenza (Mattock *et al*, 1988).

Apart from searching for the cohort effects of individual epidemics, like the 1918/19 and 1957 epidemics of influenza A, the most obvious need at present is to find out whether the year-to-year and month-to-month fluctuations in the incidence of schizophrenia reported here can be found in other large data sets. Although evidence from family, twin and adoption studies establishes beyond reasonable doubt that the main determinants of schizophrenia are genetically transmitted (Gottesman & Shields, 1982) the consistent excess of schizophrenic births in winter and spring is strong *a priori* evidence that some seasonally varying influence is also contributing to the aetiology of the syndrome, either *in utero* or in the early months after birth. The variation in the 'incidence' of schizophrenia from year to year observed here is consistent with this hypothesis, although it is easier to account for increases than for decreases. The variation in incidence from month to month and the restriction of this variation to the four consecutive months February–May is not merely consistent with the hypothesis, it is strongly supportive. It also helps dispose of the argument, revived by Lewis (1989), that the excess of schizophrenic births in the early months of the year is simply a consequence of the 'age incidence effect'.

The observed relationship between the 'incidence' of schizophrenia and unusually low temperatures six months earlier is less firmly based, for several reasons. Previous studies based on Swedish (McNeil *et al*, 1975) and English (Hare & Moran, 1981) data failed to find any relationship between the winter birth rate for schizophrenia and temperature the previous summer or autumn. Instead, Hare & Moran found an association between cold winters and schizophrenic births in the first quarter and the first half of the year, suggesting that low temperature exerts an influence around the time of birth rather than in early pregnancy. The relationship we found was also only one of 14 different time-lagged correlations examined and the effect was quite small, a reduction in mean monthly temperature in the autumn of 1° C producing only a 7% increase in 'incidence' the following spring. However, it is striking that the months of birth which are most sensitive to temperature (March–May) are the same as those in which month-to-month variation is greatest. Nor is there anything implausible about a relationship with the third month of pregnancy. It is well established that maternal rubella in the third month of pregnancy can damage the foetal brain (Hanshaw & Dudgeon, 1978) and, in any case, low temperature probably precedes rather than accompanies the putative infection or nutritional influence.

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Season of Birth in Schizophrenia

Evidence for Confinement of an Excess of Winter Births to Patients Without a Family History of Mental Disorder

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Although it is well recognised that schizophrenic patients are more often born in winter, the significance of this finding remains obscure. Data relating to season of birth and family history were analysed for 561 patients with an ICD-9 diagnosis of schizophrenia. Patients with no family history of any psychiatric disorder group were significantly more likely to be born in winter than patients with a first-degree relative affected by schizophrenia. In comparison with normal population controls, only those without a family history exhibited a significant excess of winter births, suggesting an environmental factor of greater aetiological significance in these patients.

Clues that offer a lead to the possible causes of schizophrenia are rare. One potentially useful avenue of inquiry is the well replicated finding that patients diagnosed as schizophrenic are more often born in winter. While this association has been firmly established (Bradbury & Miller, 1985; Boyd *et al*, 1986), its role in terms of the aetiology of schizophrenia remains unclear. The explanation that has gained greatest credence (Bradbury & Miller, 1985; Torrey, 1987) is that some seasonally varying environmental factor predisposes the winter-born infant to the subsequent development of schizophrenia.

Many infectious diseases (both bacterial and viral) have a seasonally varying distribution and are capable of causing infection *in utero*. Three studies have reported correlations between the seasonal prevalence of infectious diseases and the birth rates of schizophrenic patients (Watson *et al*, 1984; Mednick *et al*, 1988; Torrey *et al*, 1988). While such data may be viewed as evidence for the hypothesis of an aetiological role for environmental damage, an alternative explanation may also account for these findings: the genetic gain hypothesis (Huxley *et al*, 1964). This contends that the schizophrenic genotype confers a form of protection or robustness from potentially deleterious environmental agents, such as infectious diseases, thereby ensuring preferential survival. The excess of winter births would therefore be attributable to the low winter mortality of those with the genotype compared with controls.

Studies endeavouring to distinguish between these two explanations have focused upon family history. Since the genetic gain hypothesis assumes a schizophrenic genotype, one might expect individuals born in winter to be more likely to have a family history of the disorder. Alternatively, an excess of winter births among patients with no family history, when viewed in conjunction with the data relating to infectious diseases, might be considered as not only an explanation for the season-of-birth phenomenon but also as evidence for an environmental cause for some forms of schizophrenia. Such studies are based upon what is now referred to as the familial/sporadic distinction (Murray *et al*, 1985; Lewis *et al*, 1987). Kendler (1988) has examined the power of such a distinction assuming aetiological heterogeneity. The power of the method varies widely as a function of the proportion of cases in the population that are truly sporadic (solely of environmental aetiology). He argues that if one assumes 10% of cases of schizophrenia to be environmental then, to obtain 80% statistical power, at least 323 probands and 1722 first-degree relatives would be required to make this distinction.

Although the relationship between family history of psychiatric disorder and seasonality of birth has been examined in eight studies, seven of these used sample sizes considerably smaller than that recommended by Kendler (Kinney & Jacobsen, 1978; Lo, 1985; McNeil, 1987; Zipursky & Schulz, 1987; Baron & Gruen, 1988; Owen *et al*, 1989; Sacchetti *et al*, 1989). Additionally, none of these studies compared risk groups with normal population controls. Since the excess of winter births in schizophrenia has been established by comparing large patient samples with normal population controls, it follows that any proposed subgroup which might account for this effect should also be compared with normal population controls. It would be expected that the winter-birth excess in such a subgroup would be considerably larger than the 5–15% usually reported for large samples (Bradbury & Miller, 1985). The only controlled study which utilised a large sample ($n = 975$) was that of Shur (1982). Although frequently interpreted as support for the environmental damage hypothesis, Shur's group with low genetic risk did not differ from controls and the winter-birth deficit in the group with high genetic risk was not statistically significant.

Our study sought to test the environmental damage hypothesis by application of the familial/sporadic distinction to season-of-birth data in schizophrenia, utilising both an adequate sample size and normal population controls.

Method

From computer records, all patients admitted to St John of God Hospital, Dublin, between November 1983 and April 1988, who satisfied the ICD–9 criteria (World Health Organization, 1978) for schizophrenia were identified. Only those patients born in Ireland with a recorded date of birth for whom comparable control data and case notes were available were included in the study.

For each year 1921–70, the seasonal distribution of births of the general population in Ireland was used to calculate the expected seasonal distribution of patients born in that year. These values were subsequently summed across all 50 birth years to give the overall expected sample distribution.

Lewis (1989) has reiterated his argument that the season-of-birth effect in schizophrenia is merely due to age incidence effects. He suggests the use of a displacement test to distinguish between the effects of seasonality and age incidence. This requires, in addition to the conventional reporting period, the use of a July to June reporting period. This resulted in the exclusion of eight patients, four born between January and June 1921 and four between July and December 1970. The expected seasonal distribution was calculated for each year of birth beginning in the third quarter of 1921. These values were then summed across the 49 years of birth included.

After extracting information on date of birth, case notes were reviewed to derive family histories of psychiatric disorder, on the basis of written records of information given by patients, key relatives, or both. Patients were then classified into one of five groups:

(a) narrow band: schizophrenia in a first-degree relative
(b) broad band: schizophrenia, major affective disorder, or completed suicide in a first or second-degree relative
(c) other: alcoholism, neurotic depression or dementia in any relative
(d) no family history: no family history of psychiatric disorder in any relative
(e) insufficient data for accurate allocation to one of the above groups.

Statistical analysis was performed using the one- or two-sample χ^2 test as appropriate. In the case of the two-sample χ^2, adjusted standardised residuals (ASRs) were calculated to identify the categories responsible for a significant χ^2 value (Haberman, 1973). Seasonal excesses and deficits are expressed as the percentage difference between the observed and expected values. In addition to conventional χ^2 tests, both Edwards' (1961) and Roger's (1977) methods for testing the significance of cyclic trends were applied. The latter is considered to reduce the risk of type 1 errors when the sample size is modest. Since only season of birth (in quarters) is available for general births in Ireland, and not month of birth during all the years of the study period, correction has only been made for the minor fluctuations in the days per month.

Results

The seasonal distribution of births for the 616 patients meeting the entry criteria is shown in Table 1. Using a January to December reporting period there is an overall tendency for persons suffering from schizophrenia to differ from the control population in having a significant ($P < 0.05$) autumn deficit and a trend towards an excess of winter births. Application of Lewis's displacement test is also shown in Table 1; the results are essentially the same. Subsequent analysis, therefore, uses the larger sample and expected values based on the January–December reporting period.

The case notes of 561 patients contained sufficient information to allow assignment to one of the four family-history groups: in group (a) there were 105 patients (narrow band), in group (b) 161 patients (broad band), in group (c) 110 patients (other), and in group (d) 185 patients (no family history). In group (e) there were 55 patients (insufficient information for allocation), and these were excluded from further analysis.

Patients with no family history of any psychiatric disorder differed significantly (with overall $\chi^2 = 8.47$, $P < 0.05$, 3 d.f.) from those with a first-degree relative affected by schizophrenia in being more likely to be born in winter

Table 1
Quarterly distribution of the births of 616 schizophrenic patients compared with normal population controls

	January–March	April–June	July–September	October–December
January–December reporting period				
Observed (O)	165	168	165	118
Expected (E)	152.0	164.9	156.9	142.2
O/E × 100%	109%	102%	105%	83%
χ^2	1.11	0.06	0.41	4.11*
July–June reporting period (Lewis's displacement test)				
Observed	162	167	163	116
Expected	150.1	162.7	155.0	140.3
O/E × 100%	108%	103%	105%	83%
χ^2	0.95	0.12	0.42	4.21*

$\chi^2 = 5.69$ and $P > 0.1$ with 3 d.f.
*$P < 0.05$ with 1 d.f.

Table 2
Quarterly distribution of the births of schizophrenic patients in each family history group using the normal population as controls

	January–March	April–June	July–September	October–December
No family history ($n=185$)				
Observed (O)	61	45	44	35
Expected (E)	45.7	49.5	47.1	42.7
O/E × 100%	134	91	93	83
χ^2	5.15**	0.41	0.21	1.39
Other ($n=110$)				
Observed (O)	29	27	31	23
Expected (E)	27.2	29.4	28.0	25.4
O/E × 100%	107	92	111	91
χ^2	0.13	0.20	0.32	0.22
Broad ($n=161$)				
Observed (O)	39	45	46	31
Expected (E)	39.7	43.1	41.0	37.2
O/E × 100%	98	104	112	83
χ^2	0.01	0.08	0.60	1.02
Narrow ($n=105$)				
Observed (O)	22	39	29	15
Expected (E)	25.9	28.1	26.8	24.2
O/E × 100%	85	139	108	62
χ^2	0.52	4.23*	0.19	3.52

No history $\chi^2=7.16$ and $P<0.10$ with 3 d.f.
Other $\chi^2=0.87$ and $P>0.10$ with 3 d.f.
Broad $\chi^2=1.73$ and $P>0.10$ with 3 d.f.
Narrow $\chi^2=8.53$ and $P<0.05$ with 3 d.f.
*$P<0.05$ with 1 d.f.
**$P<0.025$ with 1 d.f.

(ASR = 2.2) and less likely to be born in spring (ASR = 2.3). When compared with the control population (Table 2),only those patients with no family history of any psychiatric disorder demonstrate a significant ($P<0.025$) excess of winter births (34%). Patients with relatives suffering from other psychiatric disorders show no differences from the general population in terms of their season of birth. Similarly, patients satisfying the broad definition of family history are indistinguishable from controls. However, patients with at least one first-degree relative suffering from schizophrenia demonstrate a significant ($P<0.05$) excess of spring births (39%) and a trend ($P<0.1$) towards a deficit of autumn births (−38%).

Table 3
Comparison of cyclical trends in births of schizophrenic patients with and without a family history of schizophrenia

Group	Number of subjects	Peak month (Edwards' test)	Peak month (Roger's test)
No history	185	March*	March*
Narrow band	105	May***	May**

*$P<0.05$.
**$P<0.01$.
***$P<0.001$.

Results of Edwards' and Roger's tests are shown in Table 3. They confirm that patients without a manifest genetic predisposition to schizophrenia are more likely to be born in winter, and those with a first-degree relative suffering from schizophrenia are born more often in spring.

Discussion

Our overall finding of a 9% winter-birth excess, although failing to attain a conventional level of statistical significance, is broadly similar to previous reports (Bradbury & Miller, 1985). The only other Irish study reported a significant excess of spring births (O'Hare *et al*, 1980); however, over the 35 years of birth studied (1921–55), O'Hare *et al* noted a shift in the birth excess from the spring to the winter months.

The application of the displacement tests (Lewis, 1989) refutes the view that the seasonality effect in schizophrenia is the result of age incidence effects. Lewis himself points out that age incidence is at its strongest among those in the earliest years of risk (i.e. 16 years of age) and is negligible in those over the age of 23 years at the time of a study. It is hardly surprising, therefore, that this effect is not evident in our sample since it includes patients born over 50 years (1921–70) with only 11.5% of the sample under 23 years of age at the time they were studied.

A number of potential pitfalls are encountered when dividing patient groups in terms of family history. Firstly, the accuracy of the history compiled is of importance; ideally such divisions should be based on individual interviews with all first- and second-degree relatives (family study method). Secondly, a problem intrinsic to the familial/sporadic distinction, regardless of the source of the information used to allocate patients to either group, is that of the relatively young age of onset of schizophrenia. It follows that in any admission sample a substantial proportion of probands will have younger siblings who may yet develop the disorder. Thirdly, the schizophrenia genotype may fail to express itself within generations of small and sometimes relatively large families. Fourthly, further problems arise in the definition of a positive family history: does one include or exclude major affective disorder in a relative, and also, what degree of relatedness to the proband should be regarded as relevant? Finally, as already noted, the power of the distinction is dependent on the sample size used. The aforementioned problems should diminish the likelihood of detecting a 'true' difference.

Our data suggest that 19% of probands (105/561) have a first-degree relative affected by the disorder, a figure similar to that reported (17%) by Baron &

Gruen (1988), who utilised the more accurate family-study method. Since not all first-degree relatives of the probands had passed through the period of greatest risk, it is possible that some of the patients may be presently misclassified as sporadic cases. Problems regarding family size are less relevant in Ireland because families tend to be considerably larger than in most other Western countries. In the current study, probands had a mean of 5.0 (s.d. 2.3) siblings. In an attempt to circumvent problems regarding which disorders and what degree of relatedness are relevant, we used both narrow and broad definitions of a positive family history and also differentiated between patients whose relatives had other disorders and those who had no family history of any psychiatric disorder. In relation to sample size, 290 probands were used in the direct comparison of those groups. This figure approximates closely to the 323 recommended by Kendler (1988), and the use of more strict criteria and large sibships both serve to decrease the size of the sample required to obtain the same power.

Our data reveal that patients with no family history of any psychiatric disorder, when compared with patients with a first-degree relative with schizophrenia, were significantly more likely to be born in the winter months and less likely to be born in the spring months. Furthermore, when compared with normal population controls, patients with no family history of any psychiatric disorder had a significant excess of winter births, the magnitude of which was 34%. If our subdivision of probands into groups approximates to relative genetic risk, it is evident that such risk is inversely related to the frequency of winter birth. Patients with a first-degree relative affected by schizophrenia exhibited a significant excess of spring births and a trend towards an autumn deficit. The autumn deficit among the narrow-band patients provides the single greatest contribution to the overall autumn deficit, although smaller deficits are also evident in the other three family-history groups. In a reanalysis of the data of Shensky & Shur (1982), the group at the highest genetic risk demonstrated a trend towards an April/May peak and, using a wider definition of high genetic risk, they reported a significant peak in May. In both Ireland and in England and Wales (Hare *et al*, 1972) most births occur in spring, followed by summer, then winter, with least births in autumn; the same seasonal pattern is demonstrated by the narrow-band group in this study. Whether or not this similarity is due to an exaggeration of the largely unknown sociobiological factors which operate in the general population, or to different factors, is a matter for speculation.

Of the eight previous studies, four found that patients at low genetic risk were more likely to be born in winter than those at high risk (Kinney & Jacobsen, 1978; McNeil, 1987; Zipursky & Schulz, 1987; Sacchetti *et al*, 1989), two studies report that those at high risk are more likely to be born in winter (Lo, 1985; Owen *et al*, 1989) and one found no difference between the two patient groups (Baron & Gruen, 1988). In the only large study with normal population controls, Shur (1982) reports a non-significant trend towards a deficit of winter births in the high-risk group and no difference between the low-risk group and controls. Spring (high risk) and October (low risk) peaks are reported in the reanalysis (Shensky & Shur, 1982). As noted, Baron & Gruen (1988) report no difference in season of birth between their patient groups. However, using a different approach they report more cases of schizophrenia among the relatives of the winter/spring born patients than among the summer/autumn born. Sacchetti *et al* (1989), employing a similar design, report more cases of schizophrenia among the relatives of schizophrenics *not* born in winter. This finding is consistent with their report that significantly more cases at high genetic risk were born outside winter. In a study confined solely to a group at high genetic risk, Machon *et al* (1983) report that more cases of schizophrenia occurred in those born in winter or in urban areas than among others. While this finding is not directly comparable with those of the above studies, because no patient group at low genetic risk was included, Machon *et al* interpret their results as support for the environmental damage hypothesis on the assumption that infectious diseases are more prevalent in the winter months and are more likely to be transmitted in urban areas.

Other studies investigating the environmental damage hypothesis have explored the relationship between season of birth and morphological abnormalities noted on cranial computerised tomography of schizophrenic patients. Of the four studies investigating such a relationship, three reported more structural abnormalities among patients born in winter/early spring that those born in other seasons (Sacchetti *et al*, 1987; Zipursky & Schulz, 1987; Degreef *et al*, 1988); a contrary finding was reported by Owen *et al* (1989).

It is clear that contradictory findings exist in terms of both the relationship between winter birth and negative family history and the relationship between winter birth and morphological brain abnormalities. However, more studies report positive than negative associations between these variables. Given this, one might anticipate that patients with no family history would exhibit more morphological brain abnormalities than patients with a family history. Lewis *et al* (1987), while conceding that this issue remains contentious, conclude that on balance such a hypothesis is indeed supported.

Precisely which environmental factor(s) might be responsible for the season-of-birth effect in schizophrenia remains a matter of debate. A variety of seasonally varying environmental factors, which are also capable of causing abnormalities of cerebral structure have been implicated. These include infectious diseases, obstetric complications, nutritional deficiencies and environmental contaminants (Torrey, 1987). As noted previously, several investigators have reported correlations between the season-of-birth effect in schizophrenia and the prevalence of certain infectious diseases. A specific relationship has been noted between diphtheria, pneumonia and influenza and the births of schizophrenic patients (Watson *et al*, 1984). Similarly, Torrey *et al* (1988) noted a significant relationship between schizophrenic births and the reported cases of measles, polio and Zoster varicella and a trend which failed to attain statistical significance was noted for influenza.

While it has been shown that some obstetric complications (e.g. toxaemia) have a seasonal variation (Pasamanick & Knobloch, 1958) and occur to excess among those subsequently diagnosed as schizophrenic (McNeil & Kaij, 1978), neither of the two studies which have investigated their relationship with season of birth in schizophrenia have found that they are over-represented in winter-born patients (McNeil, 1987; Owen *et al*, 1989). Nutritional deficiencies have been noted to be more common in winter months (Pasamanick & Knobloch, 1961) and Dalen (1975) noted a significant drop in the seasonality effect in Sweden after 1940 following the introduction of vitamin K prophylaxis. Other than this, the role of nutritional deficiencies (and environmental contaminants) remain uninvestigated as possible explanations of the season-of-birth effect in schizophrenia.

In conclusion, one of the few well replicated epidemiological findings in schizophrenia is the fact that a disproportionate number of individuals given this diagnosis are born in the winter months. While few doubt the role of genetic factors, it is accepted that environmental factors must also play a role in the aetiology of schizophrenia. Our finding that a significant excess of winter births exists only in those without a family history of any psychiatric disorder not only supports the view that an environmental factor accounts for the season-of-birth effect, but perhaps indicates it to be of greatest aetiological significance in those without a family history of the disorder.

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The Clinical Correlates of Neurological Soft Signs in Chronic Schizophrenia

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Among 16 chronic schizophrenic in-patients, all had at least one neurological soft sign (NSS), and 6 (40%) had definite neurodysfunction. NSS and TD scores were highly intercorrelated, and NSS were significantly correlated with neuroleptic drug exposure. NSS correlated positively with both positive and negative symptoms and cognitive impairment but not with cerebral ventricular size on CT. Patients with neurodysfunction had more positive and negative psychopathology, cognitive impairment and TD than those without. Cerebral ventricular sizes and family histories of schizophrenia were similar in both NSS groups. The presence of NSS may be a simple but important way of identifying a subgroup of schizophrenics with neurodevelopmental predisposing abnormalities, and vulnerability to TD.

Neurological soft signs (NSS) have been reliably documented in schizophrenia and occur with a reported prevalence of 50–60% (Heinrichs & Buchanan, 1988). Their significance, however, is unclear, and the correlation with other clinical abnormalities or outcome is variable (Kolakowska *et al*, 1985; Wegner *et al*, 1985). Nevertheless, NSS were the best single predictor of abnormalities in three modalities: neurological examination, electroencephalograph (EEG) and computerised tomography (CT) scan, in one study of 39 patients who underwent these three tests (Woods & Short, 1985). There has, however, been a surprising paucity of studies relating the occurrence of these signs to CT scan findings and two studies have been contradictory: Weinberg & Wyatt (1982) found an association with enlarged cerebral ventricles while Kolakowska *et al* (1985) did not. Furthermore, the presence of tardive dyskinesia (TD), which is increasingly suspected of indicating underlying predisposing organic factors (Waddington, 1987), has not always been taken into account in surveys of NSS. Finally, the role of neuroleptic medication continues to be debated. While the consensus view appears to be that these signs are not an artefact of medication (Mosher *et al*, 1971; Cox & Ludwig, 1979; Torrey, 1980; Woods *et al*, 1986; Liddle, 1987; Kolakowska *et al*, 1985) this has been challenged by Quitkin *et al* (1976) who, although finding no association with medication in the group of schizophrenics with most signs (those with pre-morbid asociality), did find such an association in the remaining mixed group of schizophrenics and continue to argue that this factor has not yet been adequately excluded (Quitkin *et al*, 1985).

Accordingly, we decided to study the extent and severity of NSS in a group of chronic schizophrenic in-patients who had had CT scans and also to relate these findings to the degree of psychopathology, cognitive impairment, TD, previous neuroleptic drug histories and family history of schizophrenia.

Method

A group of 16 chronic schizophrenic (DSM-III; American Psychiatric Association, 1980) in-patients (10 men, 6 women) who had had CT scans carried out as part of a previous study (King *et al*, 1985) were selected for study. Mean age of the group was 44.4 years (s.d. 12.2, range 30–68) and mean duration of illness 21.41 years (s.d. 10.64, range 5.3–41.2). The interval between the CT scan and this study ranged from two and a half to three years. The patients were examined for TD (by JLW & AW) on two occasions six months apart and on the second occasion they were also examined for the presence of NSS. TD was assessed using the Abnormal Involuntary Movement Scale (AIMS; National Institute of Mental Health, 1976) and 10 NSS: mirror movements, speech, right/left confusion, finger-to-thumb opposition, finger-to-thumb mirror movements, pronation–supination, foot tapping (right/left), face–hand (sensory inattention), graphaesthesia and hopping (right/left), were derived from those used by Quitkin *et al* (1976), Torrey (1980) and Kolakowska *et al* (1985). They were rated on a three-point scale (0 absent; 1 present; 2 marked), so that the total possible range was 0–20. 'Adventitious overflow' was excluded from the Quitkin *et al* (1976) signs since it was indistinguishable from TD. At the time of the examination for NSS the patients were also assessed for psychopathology using the Krawiecka Rating Scale (KRS; Krawiecka *et al*, 1977) as modified by Johnstone *et al* (1978), which gives four positive symptoms (hallucinations, delusions, incoherence and emotional incongruity), two negative symptoms (poverty of speech and affective flattening) and three non-specific symptoms (depression, anxiety and psychomotor retardation), and cognitive function using the Withers & Hinton Test (1971). All available information on the current and lifetime

Table 1
Raw data

Parameter	*n*	Range	Mean	s.d.
Krawiecka (positive)	16	2–16	9.3	4.66
Krawiecka (negative)	16	2–8	4.9	1.69
Krawiecka (total)	16	5–29	17.4	7.00
Withers and Hinton	14	25–104	57.3	23.52
AIMS	16	0–22	6.4	6.76
NSS	15	1–14	6.87	4.19
VBR[1] x 100	16	5.0–19.7	9.76	3.541
Neuroleptic drug treatment:				
current daily dose:				
mg/CPZ	16	200–10000	3223	3236.1
duration: years	16	3.2–26.5	14.4	8.25
Total: g CPZ	16	1069–11470	4301	2846.0

1. Ventricle : brain ratio.

neuroleptic drug treatment was gathered from the case notes and prescription cards. This was then converted to chlorpromazine (CPZ) equivalents using the tables provided by Davis (1976) and Suy *et al* (1982).

The patients' data were divided in three ways:

(a) presence or absence of family history

(b) presence or absence of TD according to Schooler & Kane (1982) criteria

(c) presence or absence of prominent 'neurodysfunction', i.e. two or more individual signs being rated two (marked).

Thus all six patients with neurodysfunction had a NSS total score of four or more; of the nine without neurodysfunction, five showed several NSS but none was present to a marked degree. The data were analysed using non-parametric statistics (Mann–Whitney *U* and Spearman's correlation coefficients) unless otherwise stated.

Results

Two patients were virtually mute and could not be rated on the Withers & Hinton test and one of these would not co-operate with the examination of NSS. One patient had a missing hand, limiting the number of NSS that could be assessed. The means, ranges and standard deviations of all the data obtained are given in Table 1 and the inter-correlation coefficients in Table 2. The comparisons of patients with and without neurodysfunction and TD are shown in Tables 3 and 4 respectively.

These patients were severely ill and cognitively impaired, on average 44 years of age, ill for 21 years and treated with high doses of neuroleptics for 14 years (Table 1). NSS scores correlated positively with both positive and negative schizophrenic symptoms and TD, and negatively with the Withers & Hinton score (Table 2). There was a positive correlation with duration of neuroleptic treatment and current neuroleptic dose but not with total lifetime exposure. However, when the six patients with the most marked neurodysfunction were compared with the rest (Table 3) it was clear that they were the most severely ill and cognitively impaired, but there was no difference in their mean cerebral ventricular size or neuroleptic drug exposure.

The presence or absence of family history of schizophrenia did not distinguish between the patients on any of the measured variables. TD and NSS were highly intercorrelated (Spearman's rho 0.96, $P<0.01$) (Table 2). TD (Schooler & Kane criteria) was found to be present on both occasions in four patients (persistent TD group) and in four additional patients on the second occasion (transient TD group). In two of the latter patients, anticholinergic drugs had been added in the interval between examinations, in a third the dose of neuroleptics had been reduced and in the fourth the involuntary movements were confined to the trunk and extremities and no oral-facial movements were detected on either occasion. There were progressively more positive, negative and total symptoms, cognitive impairment, NSS, current medication and total exposure to neuroleptics from the no TD group to the transient and persistent TD groups (Table 4). Both TD groups showed highly significant differences in NSS and cognitive impairment from those who never had TD. The increase in psychopathology was statistically significant for negative symptoms in the persistent TD group. None of the differences between the measures of neuroleptic drug exposure were statistically significant in any of the three groups.

Table 2
Spearman correlation coefficients

	Krawiecka score Negative	Krawiecka score Total	Winters and Hinton	AIMS	NSS	VBR	Treatment (duration)	Treatment (total)	Treatment (current)
Krawiecka (positive)	0.512*	0.912**	−0.602*	0.651**	0.765**	−0.001	0.581*	0.460*	0.429*
Krawiecka (negative)		0.704**	−0.643*	0.476*	0.602*	0.138	0.292	0.340	0.291
Krawiecka (total)			−0.724**	0.555*	0.862**	0.021	0.518*	0.388	0.422
Withers and Hinton				−0.803**	−0.818**	−0.207	−0.223	−0.074	−0.204
AIMS					0.964**	0.041	0.288	0.298	0.358
NSS						0.067	0.934**	0.228	0.435*
VBR							0.270	−0.117	−0.175
Treatment (duration)								0.324	−0.193
Treatment (total)									0.660**

*$P<0.05$.
**$P<0.01$.

Table 3
Comparisons between patients with neurodysfunction (2 or more neurological soft signs of marked degree) and those without

	Neurodysfunction		P*
	Present ($n=6$) mean (s.d.)	Absent ($n=9$) mean (s.d.)	
Krawiecka (positive)	11.83	7.33	0.05
	(4.75)	(4.06)	
Krawiecka (negative)	6.17	3.89	0.01
	(1.47)	(1.05)	
Krawiecka (total)	21.33	13.44	0.02
	(4.97)	(5.53)	
Withers and Hinton	33.20	70.67	0.001
	(5.67)	(17.85)	
AIMS	12.83	2.78	0.002
	(6.79)	(2.44)	
VBR × 100	10.97	9.00	NS
	(5.32)	(2.02)	
Medication			
current: mg CPZ	4894.50	2362.33	NS
	(4306.21)	(2113.06)	
duration: years	14.08	13.82	NS
	(9.47)	(8.11)	
total: g CPZ	4722.50	4179.44	NS
	(3221.56)	(2879.96)	

*Mann–Whitney U test.

Table 4
Comparisons between patients with persistent tardive dyskinesia, transient tardive dyskinesia and with no tardive dyskinesia (Schooler & Kane criteria)

	Tardive dyskinesia		
	None ($n=8$) mean (s.d.)	Transient ($n=4$) mean (s.d.)	Persistent ($n=4$) mean (s.d.)
Krawiecka (positive)	7.0	11.0	12.25
	(4.11)	(2.94)	(5.56)
Krawiecka (negative)	4.0	5.25	6.5[1]
	(1.51)	(1.26)	(1.29)
Krawiecka (total)	13.75	19.5	22.5
	(7.48)	(1.91)	(5.92)
Withers and Hinton	77.0	43.25[4]	30.0[2]
	(13.8)	(9.25)	(5.0)
NSS	3.29	9.5[4]	10.5[3]
	(1.60)	(3.42)	(2.89)
VBR × 100	9.3	7.38	13.05[5]
	(2.03)	(1.70)	(5.25)
Medication:			
current: mg CPZ	2149.88	3710.75	4881.00
	(2294.40)	(4121.03)	(4005.40)
duration: years	12.48	17.73	14.80
	(7.32)	(10.15)	(9.37)
total: g CPZ	3103.50	5100.00	5897.50
	(899.19)	(4377.80)	(3372.53)

1. Different from both 'No TD' and combined (No TD and transient TD) groups, $P<0.03$.
2. Different from 'No TD' ($P<0.02$) and combined ($P<0.006$) groups.
3. Different from 'No TD' ($P<0.006$) and combined ($P<0.04$) groups.
4. Different from 'No TD' group, $P<0.006$.
5. Different from combined group, $P<0.02$ (Student's t).

Cerebral ventricular size (VBR) did not correlate with any of the measured variables (Table 2). A significant difference was, however, found between the four patients with persistent TD and the rest ($P<0.02$) (Table 4), as previously reported elsewhere (Waddington *et al*, 1985).

Discussion

There are a number of inevitable limitations to a study of this size which means our conclusion must be tentative. Our numbers are small and therefore, although we can be confident in the positive findings of our non-parametric statistical analysis (such as the correlations between NSS, TD and cognitive impairment), a type II error may have reduced our chances of detecting other associations. There was also a delay between the CT scans of the 1985 study and the assessment of neurological status for the present study. There are very few serial CT scan studies in schizophrenia but what information is available suggests that our findings after up to a three-year interval are valid (Nasrallah *et al*, 1986; Weinberger, 1988). The information on neuroleptic drug exposure was collected from the patient's case notes and while this suffers from inaccuracies due to incomplete records and patient compliance, we assume that these apply equally to all patients with similar diagnoses and lengths and numbers of admissions, and that there has therefore been no systematic bias.

Our patients were chronically and severely ill and all had at least one NSS. If criteria similar to Kolakowska *et al*'s (1985) had been applied (i.e. two signs 'present' or one sign 'marked') 13 of our 15 patients (86.7%) would have had some degree of neurodysfunction. Using our more stringent criteria we found six (40%) of our patients had definite clinical signs of neurodysfunction. The reported prevalence of NSS varies widely, from 29% to 80% (Cadet *et al*, 1986), but our findings are similar to those reported by Torrey (1980; 49%), Kolakowska *et al*, (1985; 46%) and Woods & Short (1985; 58%). The latter authors found a much lower incidence (19%) if signs putatively attributable to age, medication or cognitive impairment were excluded.

We have confirmed a strong association with cognitive deficit in agreement with several previous reports (Mosher *et al*, 1971; Quitkin *et al*, 1976; Kolakowska *et al*, 1985; Liddle, 1987). We have also found a high degree of correlation between NSS and TD, unlike Kolakowska *et al* (1985), but in agreement with Wegner *et al* (1985) and Marsalek *et al* (1988), and Youssef & Waddington (1988) who found a higher incidence of primitive reflexes in patients with TD. While both TD and NSS were correlated with both positive and negative schizophrenic symptoms (Table 2) and patients with neurodysfunction had significantly more positive and negative symptoms than those who did not (Table 3), patients with persistent TD had significantly more negative but not positive symptoms than those who did not (Table 4). The close association between NSS and severity of psychopathology is in agreement with Mosher *et al* (1971) and Keshavan & Yeragani (1987). The latter further noted that in longitudinal studies a fluctuation in the appearance of primitive reflexes occurred with episodes of psychosis.

Those with a family history of schizophrenia could not be distinguished from those without such a history on any of the measured variables, which does not support a familial/sporadic distinction (Murray *et al*, 1985), but our numbers may have been too small to detect this. Although the VBR in our total group of patients was significantly greater than their age-matched controls ($P < 0.001$) (King *et al*, 1985), there was only one significant within-group difference in VBR with respect to the other variables measured in the present study: the presence or absence of persistent TD (Table 4). The general lack of correlation between VBR and other clinical variables, apart from TD, is consistent with several other recent reports (Williams *et al*, 1985; Owens *et al*, 1985; Romani *et al*, 1987; Smeraldi *et al*, 1987).

There was a trend for an association between NSS and neuroleptic medication (Table 2). It is possible, however, that the association with duration of treatment could be because NSS were commoner and more marked in early-onset cases (Torrey, 1980; Woods *et al*, 1986), and that the association with current medication was due to increased treatment in patients with more severe psychopathology (with which NSS were also correlated). Furthermore, there was no significant difference in the neuroleptic exposure between those patients with and those without neurodysfunction (Table 3). Unfortunately, there were inadequate numbers in this study for a multivariate analysis which is required to control for the intercorrelations between these factors. Accordingly, in agreement with Quitkin *et al* (1985), we are unable to exclude some influence of medication in the appearance of these signs.

The significance of NSS in schizophrenia is unclear. Some of the motor disturbances involved have been attributed to bradykinesia. Although this was not formally quantified in the present study, none of the patients had any clinically significant extrapyramidal signs, nor did the retardation score on the KRS differ between the patients with neurodysfunction and those without. NSS have been reported to reflect fronto-parietal (Cox & Ludwig, 1979) and fronto-temporal (Taylor & Abrams, 1984) abnormalities. Liddle (1987) thought that three separate schizophrenic syndromes could be distinguished by different symptom clusters and were associated with different patterns of cognitive deficit. He found that the two frontal lobe syndromes, the disorganisation syndrome (inappropriate affect, poverty of content of speech and thought disorder) and the psychomotor poverty syndrome (poverty of speech, decreased spontaneous movement and affective blunting) were associated with NSS, but that the temporal lobe syndrome – reality distortion (delusions and hallucinations) – was not. A high prevalence of 'harder', localising signs has also been found in both schizophrenics (Woods *et al*, 1986) and their relatives (Kinney *et al*, 1986). In spite of one report to the contrary (Cox & Ludwig, 1979), however, they do not appear to be specific for schizophrenia (Walker, 1981; Nasrallah *et al*, 1982; Woods *et al*, 1986; Gureje, 1988) and probably reflect diffuse cerebral dysfunction (Keshavan & Yeragani, 1987; Youssef & Waddington, 1988). Although there appears to be some fluctuation with severity of symptoms (Keshavan & Yeragani, 1987), there is increasing evidence from longitudinal studies of children at high risk for schizophrenia that early neuro-integrative deficits antedate and predispose to subsequent psychosis (Erlenmeyer-Kimling *et al*, 1982). A neurodevelopmental hypothesis of schizophrenia has recently been elaborated by Murray & Lewis (1987) and Murray *et al* (1988).

Our demonstration of a strong association between NSS and both TD and cognitive impairment in chronic schizophrenic patients emphasises the importance of a full neurological examination in psychotic patients (Woods & Short, 1985). Although unlikely to be of value in predicting outcome or response to treatment (Kolakowska *et al*, 1985), our findings suggest that NSS may be an important clinical means of identifying a sub-group of patients with neurodevelopmental predisposing factors which may have both genetic (Kinney *et al*, 1986) and environmental (Murray & Lewis, 1987; Cooper & King, 1987) origins, and the strong association with TD suggests that their presence might be of value in predicting vulnerability to TD.

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Sex Differences in Suicidal Behaviour of Referred Adolescents

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Reports of suicidal behaviour from four countries using the same measures were higher for girls than for boys, and higher in self-reports than in parent reports for both referred and normal adolescents. In a sample of 480 referred adolescents, patterns of 'low' and 'high' suicidal scores were different when age, sex and diagnosis were considered. The probability of high scores for girls showed only a marginal increase with age, while there was a striking rise for boys. An affective diagnosis doubled the probability of high scores for both boys and girls, while it had no effect on low scores. Psychosocial stressors also increased the probability of high suicidal scores, particularly in adolescents with an affective disorder. Sex differences in suicidal behaviour were marked in the low-scoring groups.

There is a good deal of research showing that suicidal behaviour (i.e. suicidal thoughts and/or attempts) increases markedly during adolescence (e.g. Kreitman, 1977; Shaffer & Fisher, 1981; Brooksbank, 1985; Kienhorst *et al*, 1987). Completed suicide is a relatively infrequent event which is very difficult to predict and is observed more often in male adolescents (Shaffer & Fisher, 1981; Pokorny, 1983; Goldney & Spence, 1987; Shaffer, 1988), while suicidal attempts are relatively common in this age group, particularly among women (Kreitman, 1977; Hawton, 1982). To increase our understanding of suicide and improve the management of suicide attempts, it is necessary to gain a more comprehensive understanding of suicidal ideation and attempts.

Suicidal ideation has been found in 2–26% of normal children or adolescents, depending on the criteria used; children report their own suicidal thoughts and attempts more often than parents identify such feelings or behaviour in their children; agreement between parent and child is usually poor; and suicidal behaviour is strongly and significantly related to psychiatric disorder (Joffe *et al*, 1988; Velez & Cohen, 1988). However, adolescents who attempt suicide in clinical samples seem to be a very heterogenous group (Shaffer, 1982; Khan, 1987). Although depression is an important correlate of suicidal behaviour, suicidal thoughts and attempts are common in both depressed and non-depressed groups (Carlson & Cantwell, 1982; Pfeffer *et al*, 1984; Kosky *et al*, 1986; Apter *et al*, 1988).

Despite recent evidence suggesting that psychopathology may present differently in girls and boys (Achenbach & Edelbrock, 1983; Ostrov *et al*, 1989), and despite the marked sex differences in suicidal behaviour, very little is known about the factors underlying such differences. In the present cross-sectional study we report the effects of sex, age, diagnosis and other variables in patterns of suicidal behaviour in a sample of referred adolescents.

Method

The 480 adolescents included in this study comprise all the patients for whom consensus diagnoses according to DSM–III (American Psychiatric Association, 1980) were available at the time of analysis, from all the children assessed at the Rivendell Adolescent Unit (Sydney, Australia) between March 1983 and December 1985. This group includes the 393 cases described by Rey *et al* (1989) and a further 87 who were subsequently diagnosed by consensus by the same two clinicians. Total behaviour-problem scores for this group on the Child Behaviour Checklist (CBCL; Achenbach & Edelbrock, 1983) had a mean of 72.5 and s.d. 9.5, and on the Youth Self-report (YSR; Achenbach & Edelbrock, 1987) had a mean of 58.7 and s.d. 10.9. These scores are slightly higher than corresponding scores from US referred adolescents (Achenbach & Edelbrock, 1983, 1987). The age and sex distribution is presented in Table 1. Girls were significantly older than boys ($\chi^2 = 11.8$; d.f. $= 4$; $P < 0.02$), but there were no differences between the sexes in socio-economic status. None of the subjects was an in-patient at the time of assessment; about 20% were subsequently admitted for in-patient treatment.

Table 1
Age and sex distribution of the subjects ($n = 480$)

Age	Boys		Girls	
	No.	%	No.	%
12	53	18	25	13
13	84	29	51	27
14	79	27	49	26
15	52	18	32	17
16	22	8	33	17
Total	290	100	190	100

Most referrals to the unit are from school counsellors (31%), followed by parents (22%), psychiatrists (18%), welfare workers (6%) and general practitioners (2%). The most common reason for referral is disruptive behaviour either at home or at school (25%), followed by school refusal (13%) and unhappiness/depression (12%). Suicidal behaviour is the reason for referral in 7% of the cases.

Assessment method and diagnosis have been described elsewhere in detail (Rey *et al*, 1989). Briefly, all referrals to the unit from March 1983 to December 1985 were eligible for inclusion in the study. A case was selected only if standard data were available, including the following: information from the referring agency; Rivendell Questionnaire, covering demographic, medical, developmental and school data (copy available on request); CBCL for ages 4–16, completed by the parents; YSR for ages 11–18, completed by the adolescent; and assessment report based on interview(s) with the family and the adolescent.

When information in the file was complete, two senior clinicians made independent diagnoses on the five DSM-III axes. To reach a diagnosis, the clinicians used all the information available in the file, including school reports, reports of psychological and educational testing, and parents' and children's item responses in the questionnaires (questionnaire scores, however, were not available in the file). Once the independent DSM-III diagnoses had been made, the cases in which there was disagreement on axis I were reviewed by the same two clinicians who, after further consideration of the available data, made a joint decision about which diagnostic criteria were met by the child, and the consequent DSM-III diagnosis (consensus diagnosis). This process was used with the first 393 cases; the other 87 had diagnoses made only by consensus by the same two clinicians, as described above, without prior independent diagnosis. The reason for this change was that the former group was the object of a reliability study on diagnosis (Rey *et al*, 1989). Once that study was completed and reliability estimated, it was considered unnecessary to continue doing independent diagnoses.

For the purposes of the present study the different diagnoses were grouped into four categories: affective disorders (33 girls, 28 boys) ('affective group', comprising major depression, bipolar and dysthymic disorders); disruptive-behaviour disorders (66 girls, 143 boys) ('disruptive group', comprising conduct, attention-deficit and oppositional disorders); adjustment disorders (31 girls, 47 boys) ('adjustment group'); and other disorders (60 girls, 72 boys), which includes all other diagnoses. A case was included in the affective group even if there was a concurrent diagnosis from other groups.

Chance-corrected agreement (kappa) for all independent diagnoses was 0.59; it was 0.45 for the affective group, 0.60 for the disruptive group and 0.48 for the adjustment group (Rey *et al*, 1989). Estimated reliability of consensus diagnoses (kappa with Spearman–Brown correction for two raters; Guilford, 1954) was 0.74 overall; for the affective group it was 0.62, for the disruptive group 0.75 and for the adjustment group 0.65.

Measures

For the purposes of this study, suicidal behaviour is understood as the report by parents or children of suicidal thoughts and/or self-destructive acts. Reports of suicidal thoughts or attempts were extracted from the CBCL and YSR. These are well known and widely used instruments whose reliabilities and usefulness have been reported in detail (Achenbach & Edelbrock, 1983, 1987; Achenbach & Brown, 1990). The items used here are the same as those used to report suicidal behaviour in the Ontario Child Health Study (Joffe *et al*, 1988).

Five measures of suicidal behaviour were used. One was item 18 of the CBCL and YSR: "Deliberately harms self or attempts suicide" (parent form); "I deliberately try to hurt or kill myself" (child self-report). Another was item 91 of the CBCL and YSR: "Talks about killing self" (parent); "I think about killing myself" (child). Items 18 and 91 are rated on a three-point scale (0, not true; 1, somewhat/sometimes true; 2, very true). The third measure – suicidal behaviour (child) – was obtained by adding up scores on items 18 and 91 from YSR (five-point scale, 0 to 4). The fourth – suicidal behaviour (parent) – was obtained by adding up scores on items 18 and 91 from CBCL (five-point scale, 0 to 4). The fifth – the overall suicidal score – was obtained by adding up child and parent suicidal scores (nine-point scale, 0 to 8).

Other measures considered in this study were ratings by two judges on axes IV and V of DSM-III and on a measure of chronic adversity (Psychosocial Adversity Index, PSAI). The PSAI has been described elsewhere in detail (Rey *et al*, 1987, 1988). Estimated reliabilities (intraclass correlation coefficient with Spearman–Brown correction for mean ratings of two judges; Guilford, 1954) for a subsample of 140 of these adolescents were 0.61 for axis IV, 0.73 for axis V and 0.81 for PSAI (Rey *et al*, 1987). Ratings of socio-economic status (SES) according to Australian norms (Daniel, 1983) were also used.

Results

Table 2 presents the prevalence of suicidal thoughts or attempts (rating $\geqslant 1$) according to parent (CBCL) and child (YSR) reports in our subjects, and comparative figures from four other groups: CBCL and YSR in normal and referred US samples (the characteristics of those samples were explained in detail in Achenbach & Edelbrock, 1983, 1987); parallel Dutch CBCL data for normal and referred samples (F.C. Verhulst, personal communication, 1988); CBCL data from a Sydney normal sample (described in Hensley, 1988) and YSR data from the Ontario Child Health Study (Joffe *et al*, 1988). Reports of suicidal behaviour were higher for girls than for boys, and higher in self-reports than in parent reports both in referred and non-referred subjects.

Distribution of scores in all the measures of suicidal behaviour in the Rivendell sample was very skewed, with a modal score of zero. A score of two or more points was obtained by 50% of girls and 32% of boys.

Correlations between parent's and child's reports were 0.40 for item 18 and 0.38 for item 91, while parent–child agreement (kappa) on presence (score = 0) or absence

Table 2
Prevalence (%) of suicidal behaviour (score$\geqslant$1) in 12–16-year-olds in referred and normal samples

Sample	Girls		Boys	
	parent report	child report	parent report	child report
Item 18: suicide attempts				
USA normal[1]	0.8	7.6	0	2
Dutch normal[2]	0.8	–	1.1	–
Ontario[3]	–	7.1	–	2.4
Sydney normal[4]	1.9	–	1.1	–
USA referred[1]	18.4	26.1	8.5	9.2
Dutch referred[2]	5.6	–	6.8	–
Present study	24.4	37.8	14.9	22.7
Item 91: suicidal thoughts				
USA normal[1]	0.8	16.5	1.2	8
Dutch normal[2]	0.8	–	1.3	–
Ontario[3]	–	14.5	–	3.3
Sydney normal[4]	3.8	–	1.9	–
USA referred[1]	22.9	36	14.5	16
Dutch referred[2]	19.8	–	12.8	33.6
Present study	37.9	53.7	30.3	33.6
Items 18 and 91				
USA normal[5]	1.6	18.1	1.2	8.4
Sydney normal[4]	4.7	–	2.6	–
USA referred[5]	28.3	38	18.7	19.2
Present study	44.2	56.1	34.1	37.6

1. Achenbach & Edelbrock, 1983, 1987.
2. Personal communication, F.C. Verhulst, 1988.
3. Joffe *et al*, 1988.
4. Unpublished data extracted from Sydney's normative sample (Hensley, 1988).
5. Unpublished data extracted from Achenbach & Edelbrock's normative samples.

Table 3
Likelihood-ratio χ^2 statistics for selected models

Model	Effects in model[1]	d.f.	χ^2
1	A, B, AB	6	34.20
2	A, B, AB, C_1	8	49.67
3	A, B, AB, C_1, D, C_1D	12	64.65
4	A, B, AB, C, D, CD	20	67.72

1. Variables: A, sex (dichotomy); B, age (continuous); C, diagnosis (categorical, 4 categories); C_1, affective v. non-affective (contrast across categories of C); D, axis IV (continuous).

(score$>$0) of these types of behaviour was 0.34 for both items.

The data were analysed by regressing total score on a set of predictor variables including sex, age, SES, diagnosis, axis IV, axis V and PSAI, and their interactions. Because of extreme skew and variance heterogeneity in total scores, a linear multiple regression analysis was considered to be inappropriate. Scores on the eight-point scale were categorised as zero (0; 44% of all subjects), low (1 or 2; 33% of subjects) or high (3 or above; 23% of subjects). A polytomous logit model (Aldrich & Nelson, 1984) was used to analyse the relationships between the predictor variables and total score. By treating the scale as a polytomous rather than a dichotomous variable, effects of predictor variables on variability as well as effects on level of suicidal score could be examined.

A series of model comparisons showed that some but not all of the predictor variables were associated with suicidal score. Table 3 shows χ^2 statistics associated with some of the models tested. All of the models in Table 3 provide significant predictability ($P<0.001$), but some (such as model 4) are much more complex than others (such as model 1). For any pair of the models in Table 3, the difference between the two χ^2 values can be used to determine whether the more complex model in the pair provides significantly better predictability than the more simple model. Values of χ^2 for selected model comparisons are shown in Table 4.

The most parsimonious model consistent with the data (model 3) includes sex, age, a contrast across diagnostic categories, axis IV, and two interactions: sex by age, and diagnosis by axis IV. The diagnosis contrast included in the model distinguishes between the affective diagnosis category and all other diagnoses. The comparison between model 3 and model 4 ($\chi^2=3.07$, 8 d.f.) demonstrates that distinctions among disruptive-behaviour disorders, adjustment disorders and other disorders make no significant contribution to predictability. Similarly, variables excluded from the models in Table 3 (SES, axis V, PSAI and additional interaction variables) do not produce significant increases in predictability.

We conclude, then, that suicidal scores in our population of referred adolescents depend on sex, age and their interaction, on diagnosis (affective v. other) and on severity of stressors (axis IV).

Given any of the models in Table 3, it is possible to predict for each subject in our cohort the probability of a zero, low or high suicidal-behaviour score. Probabilities based on age, sex and their interaction, ignoring diagnosis (model 1) are shown in Table 5. Table 5 also shows the effect of including diagnosis in the model, ignoring axis IV scores.

The nature of the age and sex effects can be summarised as follows. Ignoring diagnosis (model 1; Table 5): (a) with increasing age, the probability of a non-zero suicidal-behaviour score increases for girls, but decreases slightly for boys; (b) the increase for girls is due to an increase in both low and high scores, while for boys the decrease is due to an increase in the variance of scores, with both zero and high scores becoming more frequent at higher age levels; (c) at all age levels, girls are more likely than boys to have high suicidal-behaviour scores.

Table 4
Model comparisons

Models compared	d.f. difference	χ^2 difference	*P*
1,2	2	15.47	<0.001
2,3	4	14.98	0.005
3,4	8	3.07	0.930

Table 5

Probabilities of 'zero' (score = 0), 'low' (score = 1,2) and 'high' (score ≥ 3) total suicidal scores according to age and sex; model includes sex, age, and sex by age and by diagnoses

	Boys			Girls		
	zero	low	high	zero	low	high
Age 12	0.44	0.46	0.10	0.54	0.24	0.22
Age 13	0.48	0.38	0.14	0.44	0.29	0.27
Age 14	0.51	0.31	0.18	0.35	0.34	0.31
Age 15	0.53	0.24	0.23	0.27	0.38	0.35
Age 16	0.53	0.18	0.29	0.21	0.42	0.38
Affective diagnosis						
Age 12	0.25	0.53	0.22	0.28	0.26	0.46
Age 13	0.27	0.44	0.29	0.22	0.29	0.48
Age 14	0.29	0.35	0.36	0.18	0.32	0.50
Age 15	0.30	0.27	0.44	0.14	0.35	0.51
Age 16	0.29	0.20	0.51	0.10	0.38	0.52
Non-affective diagnosis						
Age 12	0.45	0.45	0.10	0.55	0.24	0.22
Age 13	0.50	0.38	0.13	0.47	0.29	0.24
Age 14	0.54	0.30	0.16	0.39	0.34	0.27
Age 15	0.56	0.24	0.20	0.32	0.39	0.29
Age 16	0.58	0.18	0.24	0.26	0.44	0.31

When diagnosis is taken into account (model 2; Table 5), it becomes clear that the above comments apply mainly to the non-affective group, largely because of the relative frequency of those diagnoses. (a) For girls with affective disorders, the chance of high suicidal scores shows only a marginal increase as age increases (0.46 at age 12 v. 0.52 at age 16), while it shows a marked rise for boys (from 0.22 at 12 to 0.51 at 16), so much so that by age 16 the probability of high suicidal scores is the same for boys and girls. (b) For both affective and non-affective groups, variability in scores increases with age for boys, but not for girls. (c) The probability of a high suicidal score is about twice as high for adolescents with affective disorders as it is for those with other disorders, regardless of sex or age.

A high axis IV score further increases the probability of a non-zero suicidal score, but the increase is greater for those in the affective group than for those with other diagnoses. According to model 3, a 14-year-old boy with an affective-disorder diagnosis and an axis IV score of 3 (one standard deviation below the mean) has a probability of 0.52 of obtaining a non-zero suicidal-behaviour score, while the probability associated with an axis IV score of 5 (one standard deviation above the mean) is 0.84. Corresponding probabilities associated with other diagnoses are 0.42 (for an axis IV score of 3) and 0.51 (for a score of 5).

Discussion

Because this research is based on a referred group of patients and not on a random sample of the general population, results will need to be replicated before they can be generalised. Nevertheless, patterns of referral to the unit, the types of presenting problem and the diagnostic mix suggest that there is no strong referral bias towards suicidal adolescents. Since diagnoses were made for other purposes and long before this study was conceived, it is unlikely that knowledge of the adolescent's suicidal behaviour would have influenced raters' diagnoses in relation to the study.

Suicidal behaviour in this referred sample is high, between 34% and 56% of cases, depending on sex and on informant, and higher than in other referred samples using the same questionnaire (Table 2). This suggests that our sample may be more disturbed overall as reflected by higher total behaviour-problem scores in the CBCL and YSR, and by the fact that 20% of cases were subsequently admitted for in-patient treatment. It may also be the result of Sydney parents and children reporting more problems (Achenbach *et al*, 1990).

Reports of suicidal behaviour in large normal and referred samples from four countries (USA, Canada, Holland and Australia) assessed with the same instrument show that children consistently report higher rates than their parents, and that girls display higher suicidal behaviour than boys in referred and non-referred samples, both in parent reports and self-reports. This is in agreement with findings in other community samples using different assessment procedures (e.g. Velez & Cohen, 1988).

One of the unresolved paradoxes in this area is that girls report suicidal behaviour more often, while boys are more likely to actually kill themselves. This conflicts with the view that there is a continuity of suicidal behaviour, from suicidal thoughts to attempts and to completed suicide. Results from this study cast some light on this topic by suggesting that there may be differences between adolescents with low and high suicidability. Although girls have a higher overall probability of 'high' suicidal scores, the slope of the increase with age is very low, while boys show a rapid rise in the likelihood of 'high' suicidal scores with increasing age. The different rates of increase of high suicidal scores for boys and girls found in our study are closer to those expected if the hypothesis of a continuity of suicidal behaviour is accepted, in view of actual suicide rates by sex and age, and therefore give some support to that hypothesis if only 'high' scores are taken into account. It remains to be seen, however, whether these trends persist into adulthood.

The relationship between depression and suicidal behaviour is a complex one, and the lack of consistent findings in the literature is likely to reflect in part the confusion that still reigns in the area of depression in childhood and adolescence and how it is defined

(Angold, 1988*a*,*b*; Nurcombe *et al*, 1989). While many young suicide-attempters are depressed and miserable, many depressed adolescents are not suicidal (Carlson & Cantwell, 1982). However, referred adolescents often complain of misery and depressive feelings and this occurs across psychiatric diagnoses (Nurcombe *et al*, 1989). For example, scores on the Children's Depression Inventory (Kovacs, 1980/81) have been unable to distinguish between adolescents suffering from conduct and affective disorders in several reports (Costello & Angold, 1988).

There is little doubt that suicidal adolescents are a heterogeneous group (Shaffer, 1982; Khan, 1987); however, this study suggests that an affective-disorder diagnosis increases the likelihood of suicidal behaviour by doubling the probability of high suicidal scores for both girls and boys, but that it has little effect on low scores. Psychosocial stressors, as reflected by scores on axis IV or DSM–III, further increase the probability of suicidal behaviour across sexes and diagnoses, but this increase is particularly marked if the adolescent has an affective disorder. These findings underscore the vulnerability of adolescents in this diagnostic group.

The main difference between boys and girls in the patterns of suicidal behaviour occurs in the 'low' suicidal score groups, suggesting that – apart from the possibility that the low-score groups may represent a different category of adolescents – this may be a gender-related phenomenon. It warrants further study.

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Using the Hospital Anxiety and Depression Scale to Screen for Psychiatric Disorders in People Presenting with Deliberate Self-harm

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In-patients referred to a deliberate self-harm team were asked to complete the HAD questionnaire and diagnoses were made using the SCID. The total prevalence of psychiatric disorder by DSM–III criteria was 54%. The HAD performed well as a screening instrument; a threshold score of eight gave a sensitivity of 88% and a positive predictive value of 80%; its use by non-psychiatrists to detect depressive disorder in patients presenting with deliberate self-harm is to be recommended.

Patients presenting with deliberate self-harm (DSH) place a considerable strain on acute medical services. Between 1961 and 1977 the annual rate of hospital discharges and deaths stemming from the adverse effects of medication had reached a worrying 10% (Alderson, 1974). DSH occurred commonly in the young, and rates based on the hospital in-patient inquiry for 1976 were 220 and 640 per 100 000 respectively for young males and females. Rates appeared to peak in the late 1970s when Diekstra (1985) calculated that throughout the EEC the total number of DSH actions was 1 400 000. During the 1980s there was a gradual reduction in the number of reported cases (Brewer & Farmer, 1985), but the impact on hospital resources is still considerable.

Reasons given for DSH are varied, and not all patients are suffering from a psychiatric disorder. However, Newson-Smith & Hirsch (1979), using the Present State Examination, found that 31% of patients had a definite psychiatric disorder and a further 29% fell within a borderline or 'threshold' category, with depression being the commonest diagnosis. Underlying depressive disorders have also been estimated as present in 70% of patients who successfully committed suicide (Barraclough *et al*, 1974). For this reason it is important that patients presenting with DSH are carefully screened for the presence of an underlying depressive disorder.

Practice varies from centre to centre depending on the availability of specialist teams, local experience, and operational policy, but not all DSH patients are referred for psychiatric assessment before leaving hospital. Social workers and nurses, after special training, have been shown to be as reliable as psychiatrists in carrying out assessments (Newson-Smith & Hirsch, 1979; Catalan *et al*, 1980). Since an important part of such assessments is screening for a depressive disorder, it was felt that a questionnaire that could alert staff to the presence of these disorders would be of value.

The Hospital Anxiety and Depression Scale (HAD) is a screening instrument for clinically relevant anxiety and depressive states (Zigmond & Snaith, 1983), which is quick and easy to administer and simple to score and interpret. There are separate seven-item scales for anxiety and depression, with a range of scores from 0 to 21. The HAD was developed for use in a hospital setting and is said to be unbiased by co-existing physical illness since it avoids inquiry about symptoms (e.g. insomnia and weight loss) which can have a physical cause. As a rating scale it has been compared favourably against the Montgomery Asberg Depression Rating Scale, the Beck Depressive Inventory and the Clinical Anxiety Scale (Snaith, 1985; Aylard *et al*, 1987). The aim of this present study was to see whether the HAD could be used to identify depressive illness in DSH patients.

Method

The assessment of DSH patients in North Lincolnshire Health Authority is carried out by a nurse from the DSH team who is usually responsible for seeing all referrals and making arrangements for follow-up, admission or urgent further opinion as indicated by her assessment. For the purposes of this study each of 100 consecutively referred DSH patients were, in addition to their normal assessment, asked to complete the HAD questionnaire and to be interviewed using part of the Structured Clinical Interview for DSM-III (SCID) relevant to anxiety and depressive disorders (Spitzer, 1983). The SCID is an instrument used to gather information in a systematic way in order to make psychiatric diagnoses according to DSM-III criteria (American Psychiatric Association, 1980).

Patients were excluded from the study if they were assessed by anyone other than the DSH nurse or if they were too drowsy to complete the questionnaire. The mode of disposal for each patient was also noted. All decisions about disposal were made blind to the DSM–III diagnoses and HAD scores, which were only calculated at the end of the study. In order to validate the diagnoses made by the nurse, 20% of the patients were also interviewed separately by an experienced psychiatrist using the same instrument blind, until the completion of the study and the DSH sister's assessment.

Results

In total, 100 patients completed the HAD questionnaire and were diagnosed according to DSM-III criteria. No one who was approached refused to be interviewed. Twenty-eight patients were also interviewed by the research psychiatrist. Of the patients, 60% were female and the population mean age was 33.5 (s.d. 14) years. Marital status of the study population was as follows: 35% married or cohabiting, 37% single, 22% divorced or separated, and 6% widowed. Fifty-four per cent were diagnosed as suffering from a psychiatric disorder by DSM-III criteria and the diagnoses made were as follows: 48% major depressive disorder, 2% dysthymia, 4% generalised anxiety disorder. In those patients assessed by a psychiatrist there was agreement about the diagnosis in 24 out of 28 cases (86%). Diagnoses made by nurse and psychiatrist were compared and no statistical difference was found ($\chi^2=41.8$, d.f. 3, NS).

Using DSM-III criteria of major depressive disorder and dysthymia as a yardstick, the effectiveness of the HAD as a screening tool was measured. The sensitivity, specificity and positive predictive value were calculated using different cut-off scores. In view of the very small number of anxiety disorders in the study, the HAD's effectiveness at screening for such disorders was not examined.

To test the effectiveness of the HAD at screening for depression, receiver operating characteristics (ROC) curves were plotted (see Fig. 1).

It can be seen that the curve produced is well away from the diagonal, indicating good discrimination between cases and non-cases defined by DSM-III criteria. The cut-off score which gives the best compromise between sensitivity and false positive rate, that is, the point furthest from the diagonal, is 8. A cut-off score of 8 appears to offer the best compromise between sensitivity (88%) and specificity (78%). The positive predictive value is the probability of a case defined by the questionnaire being found a case by DSM-III criteria, and this was 80% when a cut-off score of 8 was used. Increasing the cut-off score to 11 results in a high specificity (95%) but at the cost of a much reduced sensitivity (67%), while lowering it to 7 results in a higher sensitivity (90%) but reduced specificity (72%).

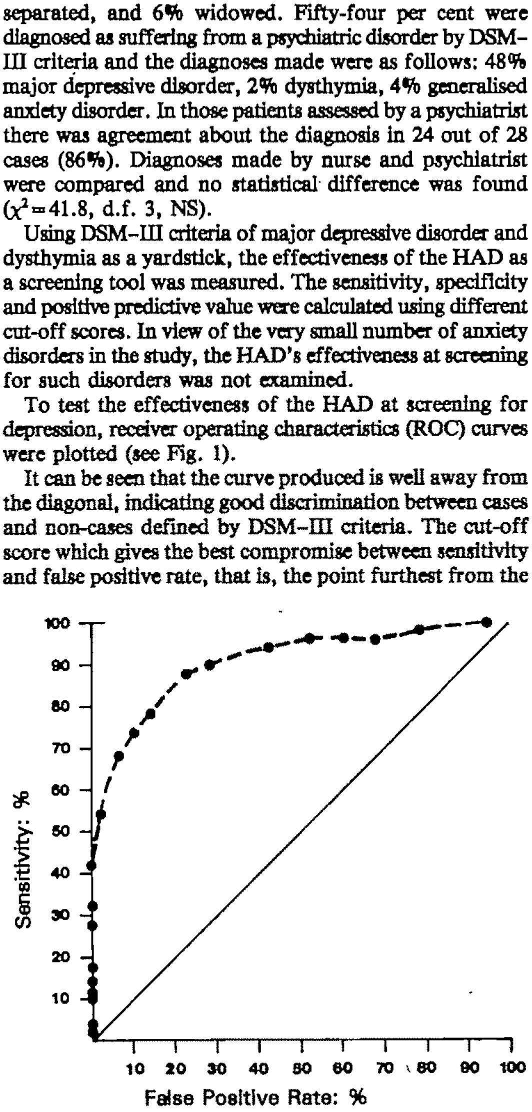

Fig. 1.

Most patients were offered some form of follow-up appointment, although 20% were discharged back to primary care; 75% of such cases had no psychiatric illness. Follow-ups were performed by a psychiatrist (63%), a community psychiatric nurse (13%) and a social worker (4%). Decisions made by the nurse regarding disposal appeared appropriate – only 4% of cases subsequently diagnosed as depressed by DSM-III criteria did not have medical follow-up of some kind.

Discussion

The incidence of major depressive disorder in this study appears rather high at 48% when compared with other studies; for example, Newson-Smith & Hirsch (1979) found that only 31% of patients had a definite psychiatric disorder. Urwin & Gibbon (1979) found rates of 30% and 42% respectively for definite and possible psychiatric disorder. These differences may reflect the differing diagnostic systems that were used: DSM-III v. PSE-CATEGO. However, the high level of agreement between diagnoses made by the nurse and research psychiatrist (24 out of 28) would support the view that the sister performed as well as the psychiatrist in diagnosing psychiatric disorder using a standard interview schedule. The SCID appears to be an interview technique that might well be successfully taught to staff who have to assess DSH patients and detect psychiatric disorder.

ROC curves are plots of true positive (sensitivity rates) against false positive (the complement of specificity rates). This form of analysis was originally devised to examine variations in radar operators' abilities to discriminate between signals and background noise. It has been shown to be useful in clinical epidemiological studies (Erdreich & Lee, 1981). The curve demonstrates the discriminating power of the questionnaire for every possible threshold score and if this is no better than chance the resulting curve is a diagonal straight line rising from the origin. If discrimination is better than chance then the curve is bowed upwards from the diagonal in relation to this power, the perfect curve being one which reaches up to the point where sensitivity is 100% and a false positive is 0%. The point on the curve which is furthest from the diagonal can be taken as the best compromise between sensitivity and specificity. The authors of the HAD recommend using a HAD Depression (D) score of 11 or more as a criterion of a probable case of depression with a score of 8 to 10 indicating a possible case. The final decision about what score to use as a cut-off will depend on whether cases must be identified whatever the rate of false positives (high sensitivity, low specificity) or vice versa. However, findings of a HAD D score of 8 being the optimal threshold for detecting a depressive disorder is similar to that seen in other studies (Andrews *et al*, 1988; Barczak *et al*, 1988; Wilkinson & Barczak, 1988). This is in accord with the original author's recommendation that a cut-off score at the lower end of the borderline range (8 to 10) be taken when the HAD is used as a screening instrument and it is important that all cases be identified (Snaith, 1985). In the case of DSH assessment, if the HAD were to be used as a means of identifying those patients requiring treatment for depression, it would seem reasonable to be over-inclusive rather than under-inclusive and so the use of the lower score of 8 is justified. Although the HAD scale was first devised as a way of detecting clinically significant depression in patients with physical illness, the present study indicates its usefulness across a range of clinical situations.

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Treatment as an Alternative to Prosecution: Offenders Diverted for Treatment

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In Scotland, procurators fiscal (state prosecutors) can divert certain offenders from the court process into treatment. This paper describes the first diversion scheme in which offenders who are suspected of having psychological difficulties are referred for psychological and psychiatric treatment before, and generally in lieu of, prosecution. It is argued that the procurator fiscal is successful in selecting suitable cases for treatment: most people referred have significant psychological difficulties but have failed to obtain appropriate assistance through the normal channels of referral.

Within the Scottish legal system, procurators fiscal (state prosecutors) make complex decisions about accused people: their decisions are not merely focused on whether or not to prosecute. 'Primary diversion' is a procedure by which the procurator fiscal can remove accused people from the normal process of prosecution if he believes that their offences were linked to psychological disturbance. This paper describes the first scheme of this kind in Scotland.

Publication of the Stewart Committee Report (Her Majesty's Stationery Office, 1983) acted as a stimulus for the establishment of a scheme whereby individuals could be sent for psychological and psychiatric assessment before the decision to prosecute is made. On receiving a police report which suggests that the alleged offender is psychologically disturbed or that the offence is out of character, the procurator fiscal may refer the alleged offender to forensic services at the Douglas Inch Clinic in Glasgow. Cases are allocated to either clinical psychologists, psychiatrists, or social workers, depending on the nature of the apparent problem and the particular expertise of the clinician involved. During an assessment interview the clinician determines the role which psychosocial factors may have played in the alleged offence. The person's state of mind at the time of the offence, contemporaneous stresses or difficulties in his/her life and perhaps problems of addiction are described. In addition, the clinician guides the procurator fiscal not only about the availability of a suitable treatment regime, but also about the patient's motivation to comply with this treatment regime. If the patient is clearly in need of help, but his motivation appears to be poor, then the clinician can suggest that the decision to prosecute might be usefully delayed for some three months.

When the procurator fiscal receives the clinician's assessment report he may deal with the case in several ways; he may proceed with a prosecution, he may issue a warning letter, he may terminate the process and advise the accused to attend for treatment, or he may inform the accused that he will defer his decision about prosecution for three months until he can determine the effect of treatment. The process is described in detail elsewhere (Cooke, 1990, 1991).

This scheme broadens the type of service available to those accused of offending and who are suspected of having a psychological or psychiatric difficulty. There is considerable evidence that a proportion of those awaiting trial within prison evince a high rate of psychiatric disturbance (Taylor & Gunn, 1984), and psychiatric assessment may be available to certain of these individuals (Chiswick *et al*, 1984). The diversion scheme broadens access to forensic services in two ways: firstly, those accused of less serious offences are considered (Her Majesty's Stationery Office, 1983), and secondly, the level of psychological disturbance leading to referral is lower. Since the scheme began in 1984 some 700 patients have been referred. This paper describes the types of individual who were diverted and the offences with which they were charged.

Method

In order to provide a detailed description of those who were diverted to the Douglas Inch Centre, a consecutive cohort of individuals, referred by the procurator fiscal, was interviewed by a research psychologist, either immediately before or after their interview with the clinician who was assessing their suitability for treatment.

A semistructured interview was developed for this study. It lasted between 1 and 2 hours and the following information was collected.

(a) demographic characteristics were assessed using the techniques of government social surveys (Atkinson, 1971). The distribution of members of the cohort in terms of sex, age, socio-economic status, employment status, marital status, size of household, educational level and religious affiliation were collected. Socio-economic status was defined using the criteria of Goldthorpe & Hope (1974).

(b) the presence and nature of psychiatric disturbance or personality disorder was assessed using the Schedule for Affective Disorders – Life Time Version (SADS–L; Spitzer *et al*, 1978). The psychiatric status of those referred was defined using the Research Diagnostic Criteria (RDC; Spitzer *et al*, 1978).

(c) given that the principal justification for referral to this type of diversion scheme is that the offence was prompted or influenced by psychological factors, a 60-item semistructured interview was developed to examine opportunity and motivation. The Opportunity and Motivation for Offence Questionnaire was developed to measure the following motivations for offending: impulsivity, peer pressure, tension reduction, self-esteem, accidental offending, disinhibition, excitement and material gain. Opportunity for offending was assessed in terms of objective risk of detection and the ease of committing the offence (Cooke, 1990).

(d) information pertaining to current and ongoing stresses was collected using the Life Events and Difficulties Schedule (Brown & Harris, 1978). Results pertaining to life events are published elsewhere (Cooke, 1990).

Results

In the period between March 1985 and July 1986, 150 individuals were referred under the diversion scheme. Only 8% of those who were offered the option of diversion by the procurator fiscal refused this option.

One measure of the appropriateness of these referrals is the number who were offered care at the Douglas Inch Centre or who were directed to other specialist services. Assistance was offered to 69% of those referred: 45% were offered treatment at the Douglas Inch Centre, 19% continued treatment elsewhere and 5% were referred to other treatment agencies.

If the proportion of those offered help is considered in relation to their offence category, it becomes clear that individuals who commit certain types of offence are more likely than others to be offered help (Table 1). When those accused of shop-lifting and those accused of committing a breach of the peace are compared, in turn, with all other accused, significant differences emerge: individuals accused of shop-lifting are more likely to be offered help ($\chi^2 = 13.03$, $P < 0.001$), while individuals accused of committing a breach of the peace are less likely to be offered help ($\chi^2 = 17.60$, $P < 0.001$). There is a tendency for those accused of committing sexual offences to be offered help more frequently than others, but, this effect fails to achieve statistical significance ($\chi^2 = 2.95$, NS). Given that 88% of the sex offenders were offered help, the failure to achieve significance probably reflects the small size of this subgroup.

If the sex distribution of those who received help is examined, it emerges that females are significantly more likely to be offered help than males ($\chi^2 = 7.83$, $P < 0.01$). This can be explained, to some extent, in terms of sex differences in the distribution of offences: more females were accused of shop-lifting, more males were accused of committing a breach of the peace.

Of these 150 individuals, 111 were interviewed for the research study. This represents a contact rate of 74%.

Males comprised 52% of the cohort. It would appear, therefore, that women diverted from prosecution are over-represented. This sex ratio of virtually 1:1 should be contrasted with a male:female ratio of 8:1 for those who are proceeded against in Scotland (Her Majesty's Stationery Office, 1987).

The age distribution of the cohort also suggests that it contained an unusual group of offenders. Individuals aged 50 years or over comprised 36% of the cohort, while those aged 19 or under comprised only 18%. It is clear that older individuals are over-represented when this distribution is compared with the distribution of convictions in Scotland (Her Majesty's Stationery Office, 1987) ($\chi^2 = 57.95$, d.f. 1, $P < 0.001$). The majority of these patients (58%) were first offenders, most having taken to criminal behaviour later in life. The proportion of cohort members who were unemployed was 66%. Of these, 75% had been out of work for three years or more.

Social class was trichotomised into high, intermediate and low (Goldthorpe & Hope, 1974). The high group comprised 11% of the cohort, the intermediate group 43% and the low group 46%. Suitable comparison statistics of the social

Table 1
Patients offered treatment at the Douglas Inch Centre or other facilities by offence and by sex (includes those not interviewed by researchers)

	Shop-lifting	Breach of the peace	Drunk and incapable	Sex offence	Offences against person	Other	Total No.	Total %
Males								
Offered help	6	17	3	14	3	4	47	59
Not offered help	2	24	3	2	1	1	33	41
Total	8	41	6	16	4	5		
Females								
Offered help	38	8	2	0	0	8	56	80
Not offered help	4	4	0	0	3	3	14	20
Total	42	12	2	0	3	11		

class distribution of offending in Scotland are not available, and so it is difficult to determine whether there is any particular class bias in the referral pattern. There is a danger that diversion could be misused as a means of keeping individuals of high social class out of the prosecution system. This does not appear to have happened because only 11% of the cohort fell into this category.

The proportion of cohort members who were married for the first or second time was 41%, and 34% were single. This distribution probably reflects the age structure of the cohort.

The Stewart Committee indicated that, in general, diversion schemes should be restricted to those accused of committing minor offences (Her Majesty's Stationery Office, 1983). More than a third of the cases were accused of theft by shop-lifting; just under a third were accused of breaches of the peace, while the remaining third were distributed among four other offence categories (Table 1). Table 1 shows that most (84%) of those accused of shop-lifting were female, while most (78%) of those accused of a breach of the peace were male. All those accused of shop-lifting were over the age of 35 years; while the majority (60%) of those accused of breach of the peace were under 35.

Of the alleged offenders, 70% had one or more formal psychiatric diagnoses (RDC). These individuals can be regarded as psychiatric cases. It is possible for an individual to be suffering from more than one disorder at any one time. For example, a diagnosis of alcoholism frequently occurred with other diagnoses, including antisocial personality, generalised anxiety and a range of depressive disorders. Where multiple diagnoses exist it is frequently impossible to determine which diagnosis is in any sense primary.

Table 2
Distribution of diagnostic categories of those interviewed

Diagnostic category	No.	%[1]
Single diagnoses		
Schizophrenia	2	2
Depressive disorders	12	11
Anxiety disorders	18	16
Personality disorder	3	3
Alcoholism	8	7
Drug abuse	4	4
Multiple diagnoses		
Anxiety with depression	5	5
Alcoholism with anxiety	5	5
Alcoholism with depression	12	11
Personality disorder with depression	3	3
Personality disorder with other diagnosis	6	5
No diagnosis	33	30
Total	111	100

1. Percentages do not add up to 100 due to rounding error.

Table 3
Distribution of diagnostic categories by sex

Diagnostic category	Male		Female	
	No.	%	No.	%
Schizophrenia	2	3	0	0
Depressive disorders	13	23	25	37
Anxiety disorders	10	18	24	36
Personality disorder	7	13	5	7
Alcoholism	16	29	12	18
Drug abuse	8	14	2	3
Total number of diagnoses	56	-	68	-
Total number of cases	35	-	43	-

In 55% of the cases there was a single RDC diagnosis, while in the remaining 45% there were multiple diagnoses (Table 2). Schizophrenic disorders were infrequent, with only two cases being identified. Of the single diagnoses, anxiety and depressive disorders were the most common. Alcoholism and drug abuse occurred less frequently, and single diagnoses of personality disorder were almost as unusual as diagnoses of schizophrenia.

Among the multiple diagnoses, cases of alcoholism in combination with anxiety or depression were most frequent. Personality disorder in combination with various other difficulties such as depression, drug abuse and alcoholism was the next most common pattern of disorder.

Differences were apparent in the sex distribution of diagnostic categories (Table 3). Case status was applicable to 60% of the males in the cohort, compared with 81% of the females. This difference is statistically significant ($\chi^2=4.78$, d.f. 1, $P<0.05$). Alcoholism and drug abuse were the most frequent diagnoses for males; depression and anxiety disorders the most common for females.

Among the individuals with formal psychiatric diagnoses, interesting variations were observed in the proportions committing particular offences (Table 4). Of those accused of theft by shop-lifting, 76% had case status, as did a high proportion of those accused of offences against the person and, to a lesser extent, those accused of minor sexual offences. A smaller proportion of those accused of being drunk and incapable or of 'other' offences had case status.

Table 4
Distribution of offence category by presence and absence of psychiatric diagnosis

	Theft by shop-lifting	Breach of the peace	Drunk and incapable	Sex offences	Offences against person	Other	Total
Case	32	23	3	7	9	4	78
Non-case	10	12	4	3	1	3	33
Total number of subjects	42	35	7	10	10	7	111
Cases as % of subjects	76	66	42	70	90	57	-

Table 5
Distribution of offence category by diagnostic category

Diagnostic category	Theft by shop-lifting	Breach of the peace	Drunk and incapable	Sex offences[1]	Offences against person	Other[2]
Schizophrenia	0	1	0	0	1	0
Depressive disorders	17	10	0	3	5	2
Anxiety disorders	25	5	0	3	3	0
Personality disorders	1	6	1	0	3	1
Alcoholism	6	13	2	2	3	2
Drug abuse	1	4	1	0	2	1

1. Indecent exposure and lewd and libidinous behaviour.
2. Includes offences against property.

When diagnostic categories were considered in relation to offence categories, other patterns emerged (Table 5). Depressive and anxiety disorders were the most frequent diagnoses of those accused of theft by shop-lifting, while the diagnosis of alcoholism was comparatively rare for this offence. Among individuals accused of committing a breach of the peace, alcoholism appeared more frequently, but in addition a substantial proportion were suffering from depressive disorders. For other offences no clear patterns emerged other than that those accused of offences against the person fell into a diverse range of diagnostic categories.

The distribution of psychological factors was examined across the cohort (Fig. 1). It appears that most offences were related to one cluster of factors, namely impulsivity, lack of control and disinhibition due to substances. There was little evidence that the offences resulted from emotional needs, including excitement, tension reduction, improvement of self-esteem or reduction in peer pressure. Indeed, with regard to peer pressure, 74% of the offences were inconsistent with the values of the offenders' peers. The desire for material or financial gain appeared to be relevant in only 4% of the cases.

For 93% of the cohort, the offence was simple to commit, there was 'easy access' and there were no significant barriers to committing the offence. In 60% of the cases the probability of being detected, the objective risk, was low.

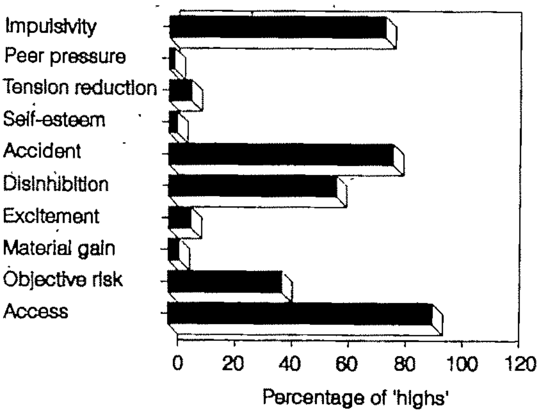

Fig. 1 Psychological factors underpinning alleged offence.

Discussion

This diversion scheme is a novel way of dealing with certain offenders. The evidence presented above indicates that patients referred under the diversion scheme are an unusual group of offenders: most of those diverted were first offenders; those who had offended before had offending histories which were significantly less serious than those of the non-diverted cases (Cooke, 1990). Many of the first offenders were older, half were female; this suggests that they were outside the normal pattern of offenders. They started offending late in life. Female shop-lifters displayed the highest rate of caseness and were the most likely group of patients to receive treatment.

The large proportion of women in the cohort, and the high rate of caseness among these women, may reflect two processes: the higher prevalence of psychological disturbance among women in the general population in Glasgow (Cooke, 1981, 1982), and the procurator fiscal's tendency to look for psychological explanations when females offend (Moody, 1983). It may be that, because women commit offences less frequently than men, those women who do commit crimes are regarded as having psychological difficulties. 'Deviant deviancy' – an individual committing deviant acts which are not usual in his/her social group – has been regarded as a pointer towards psychological disturbance. Rosenfield (1982), in a sociological account of deviance and psychiatric illness, argued that deviant behaviour which is inconsistent with sex-role expectation, particularly if that behaviour is defined as more normal for the opposite sex, is construed as more problematic and, by implication, more in need of special explanation. Certain forms of female offending may fall into this category of 'deviant deviance', and may thus contribute to the higher than expected proportion of females referred.

The finding that a high proportion of the patients were unemployed is not unexpected. Farrington *et al* (1986), reporting on the criminal behaviour of individuals followed longitudinally across many years, demonstrated that when the individuals were employed they committed fewer crimes than when they were unemployed. Unemployed individuals may have more opportunity to commit crime; they may use criminal activity not only as a means of obtaining money and material comforts, but also as a means of combating boredom.

The pattern of psychological factors which emerged suggested that the offences committed by these individuals were unplanned and impulsive. The situational factors indicated that the offences were easy to commit and the risk of detection was low. Not surprisingly, disinhibition due to the use of substances, in particular alcohol, played a significant part in the committing of many of the offences; this proportion is particularly high in this sample because of the number of people who were accused of being drunk and incapable. There was little evidence that these individuals sought to gain, materially, from their offending. This pattern of impulsive non-instrumental offending is consistent with the pattern of psychological disturbance and indicates that the procurator fiscal is selecting individuals whose offending behaviour is linked to emotional factors rather than instrumental factors.

Diversion schemes have been established for both financial and humanitarian reasons (Her Majesty's Stationery Office, 1983; Ancram, 1984): they are primarily designed to save court time and court costs. If there are any savings in court costs it will result because the care, and thereby the costs, of a particular case are being transferred from the criminal-justice system to the National Health Service. Should the National Health Service absorb these costs? The evidence available from the analysis of the cohort interviewed at the Douglas Inch Centre indicates that 70% were suffering from one or more psychiatric disorders at the time of the interview. Some of these difficulties may have been in response to their having been charged with an offence, but a large proportion of the psychological difficulties predated the offence: evidence of psychological disturbance was observed by the police officer at the locus of the offence. Only 19% of the cohort were receiving assistance for their psychological difficulties at the time of referral by the procurator fiscal; 69% were offered help by the clinicians at the Centre. It would appear, therefore, that the normal processes of referral were failing to channel these individuals to the services which they required. It can be argued that the procurator fiscal's department acted as a channel through which psychologically disturbed and distressed individuals could be referred to appropriate services.

The Douglas Inch Centre diversion scheme has been operating for five years. It appears from the evidence presented that the procurator fiscal is successful in identifying suitable offenders with significant psychological difficulties. Evidence to be presented elsewhere indicates that individuals who have been treated under the scheme have a very low rate of re-offending. What policy implications does this scheme have for the development of similar schemes both within Scotland and elsewhere?

It is important that diversion schemes are flexible; not only flexible in the way in which they are established, but also flexible in the way in which they operate. When a scheme is being established it is important that the mode of operation of the scheme evolves through discussion among all the professionals involved. Many professional groups are involved in diversion schemes of this type: they have different priorities and different concerns. Initially, members of the procurator fiscal's department may emphasise the protection of the public interest, whereas the mental health professionals may be more concerned with confidentiality and clinical effectiveness.

Issues relating to confidentiality must be resolved. The problems of clinical confidentiality can be of central importance; for example, whether the information obtained during a clinical interview can be used 'against' the patient; whether the accused must admit guilt before proceeding with treatment, and if he does so, whether the clinician must tell the procurator fiscal. Problems of this type must be clarified before the scheme can operate effectively. It is difficult to prescribe rules that will suit a diverse group of professionals working in a wide range of settings. A flexible working arrangement has to evolve through discussion over time.

Flexibility remains important when the diversion scheme is fully operational. Diversion schemes should be structured in a manner which preserves the delicate balance between three factors: the public interest, the rights of the accused, and clinical effectiveness.

Is diversion unfair to the public?

Two of the most vociferous critics of diversion schemes, McKittrick & Eysenck (1984), have argued that diversion schemes fail to preserve the public interest and violate the rights of the accused:

> "the public interest, the rights of victims, are not seen as relevant to their decision making. In other words the scheme is overwhelmingly offender orientated, the public interest is notionally protected by the fiscal, but there

> is no opportunity for the court to strike a balance between these competing interests. . . . Diversion not only diverts the alleged offender from the courts but automatically deprives him or her of the benefit of legal advice." (p. 379)

The Douglas Inch Scheme was designed to maintain a careful balance between the public interest and the rights of the accused.

It can be argued that the public interest is protected in three ways. Firstly, only a few, specially selected, individuals are diverted from the normal course of prosecution towards treatment. During the study period only 0.16% of the cases referred to the Procurator Fiscal's Department were referred on for assessment and treatment (Cooke, 1990).

Secondly, the public interest is protected because the procurator fiscal has the option to defer his decision to prosecute for three months, during which time the patient attends for treatment. Thus, contrary to McKittrick & Eysenck's contention, the fiscal can impose sanctions if the offender, having agreed to be diverted, fails to comply with treatment. This option must be used sensitively: the clinicians and the procurator fiscal frequently discuss its use in individual cases. Where the clinician suspects that the patient is using diversion as a way of avoiding prosecution – without having any real desire to tackle his psychological difficulties – the clinician may suggest that the procurator fiscal retains his right to reconsider his position in three months. This may enhance the patient's motivation towards change. Where the clinician considers that the patient has strong motivation towards treatment, and the threat of prosecution is so anxiety-provoking that it interferes with treatment, the clinician will recommend to the procurator fiscal that the diversion process should be terminated. Careful consideration of each case allows the public interest to be protected.

Thirdly, the public interest is protected because, even after the subject is referred for assessment under the diversion scheme, he can still be subject to legal penalties. Of those referred under the diversion scheme, and found unable or unwilling to co-operate with treatment, 28% were subjected to other penalties. Also, 27% received warning letters and 1% were fined.

Is diversion unfair to the alleged offender?

McKittrick & Eysenck's second major criticism of diversion schemes is that the alleged offender may be put under undue pressure to participate in treatment "when a legal adviser would manifestly advise that there is a defence to the allegations" (p. 379). When the Douglas Inch Centre diversion scheme was established, all those involved were aware of this problem. Thus, safeguards were built into the scheme. The major safeguard was the procurator fiscal's forceful suggestion, contained in the initial letter to the accused, that the accused should seek legal advice before accepting the option of diversion.

When the accused came to be assessed at the clinic, their rights were further protected. As a preamble to the assessment, the clinician would explain the purpose of the interview – to assess whether the person had a problem with which they wanted help – and if they had any doubts they would be advised to seek legal advice. The subjective impression gained from assessing and treating these individuals was not that they felt coerced into coming for treatment, but rather that they were relieved to have access to specialised treatment facilities.

If new diversion schemes are established, it is important that they can operate in a flexible manner in order to ensure that the balance is maintained between the public interest, the rights of the accused and clinical effectiveness.

Conclusion

This diversion scheme represents a valuable development in forensic services. The procurator fiscal is successful in selecting suitable cases in that he can identify people with significant psychological problems. The people who are referred generally have not received help for these psychological difficulties through the normal channels of health care and it is therefore appropriate that the procurator fiscal's department should act as a conduit through which they can obtain assistance. It is hoped that this scheme will act as a stimulus for other diversion schemes within the UK.

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Compulsory Psychiatric Treatment in the Community

I. A Controlled Study of Compulsory Community Treatment with Extended Leave under the Mental Health Act: Special Characteristics of Patients Treated and Impact of Treatment

TOM SENSKY, TIMOTHY HUGHES and STEVEN HIRSCH

Following in-patient psychiatric treatment under Section 3 of the Mental Health Act, some patients have in the past remained on Section after discharge, and subsequently the Section has been renewed while the patient remained 'on leave'. People treated thus with 'extended leave' probably resemble closely those who would be placed on a community treatment order if this were available. A group of these extended-leave patients was compared with a control group, matched for age, sex and diagnosis, selected by consultant psychiatrists as not requiring treatment using a community treatment order. The two groups showed very few differences, but the extended-leave patients more commonly had a history of recent dangerousness and non-compliance with psychiatric treatment. Use of extended leave improved treatment compliance, reduced time spent in hospital, and reduced levels of dangerousness.

The success of community care depends in some instances on the willingness of people vulnerable to serious psychiatric breakdown to co-operate with their treatments. Some people with a past history of serious psychiatric disorder (notably schizophrenia or other psychoses) can be maintained relatively well while they continue taking medications and participating in other aspects of their planned treatment. However, such individuals discharged from hospital into the community are sometimes unwilling to continue with their treatment programmes (Serban & Thomas, 1974). This has given rise to a small population of 'revolving-door' patients (Rosenblatt & Meyer, 1974; Kastrup, 1987) who repeatedly require admission to hospital, often as involuntary patients, when relapse follows their discontinuation of medication. This issue is particularly relevant for those people whose mental disorder puts them at risk of serious harm to themselves or others. The needs of such patients have given rise to much discussion in Britain and elsewhere regarding compulsory treatment orders in the community (Rohde, 1984; Mental Health Act Commission, 1986; American Psychiatric Association, 1987; Royal College of Psychiatrists, 1987; Dyer, 1987; Dedman, 1990).

Community treatment orders for people with psychiatric disorders involve complex ethical and legal issues. A major argument favouring such an order is that it would make effective treatments available to some people whose illnesses or disabilities cause them to decline such treatments. The rights of people suffering from psychiatric disorders to receive treatment have been stressed in this context (Rachlin *et al*, 1975; Gunn, 1984; Turner, 1988). However, availability of a community treatment order also poses a potential threat to the individual's civil liberties.

Before such issues can be adequately debated, several fundamental questions need to be answered. Firstly, is it possible to recognise particular characteristics of the group of individuals likely to be treated using a community treatment order? Secondly, what evidence is there that a community treatment order could be effective in psychiatric management? Thirdly, will psychiatrists (as those making medical recommendations for such an order) agree among themselves about the use of such an order? The first two questions form the main focus of the present study. The third question is dealt with in the accompanying paper (pp. 799–804).

In the UK, the question of compulsory psychiatric treatment in the community is particularly topical, given the current initiatives on community care (Department of Health and Social Security, 1989). However, this issue has wide relevance in psychiatry. Community treatment orders are already in use in some countries, notably parts of the USA and Australia. Their use has been subject to surprisingly little research. Available data are inconsistent and cannot easily be extrapolated to deal with questions relevant in the UK. In the USA, it has been estimated that out-patient treatment orders constitute up to 20% of all cases of compulsory psychiatric treatment (Miller, 1985). However, some states of the USA have used the community treatment order as "the least restrictive alternative to involuntary hospitalization"

(Hiday & Goodman, 1982), rather than a component of psychiatric management for which there are specific indications, as is intended in the UK. The decision in favour of compulsory out-patient treatment can in some instances be reached against clinical advice through legal negotiations equivalent to plea bargaining (American Psychiatric Association, 1987). Also, unlike the situation in the UK, hospital-based and community-based psychiatric facilities in parts of the USA are completely independent of each other, which sometimes gives rise to difficulties in co-ordinating (and even agreeing) individual treatment plans (Miller, 1981).

Similar difficulties arise in interpreting studies from the USA aiming to examine the likely efficacy of compulsory community treatment. Furthermore, some advocates of compulsory community treatment have based their conclusions on largely anecdotal evidence, others on studies which have been of unsound method. For example, Hiday & Goodman (1982) and Zanni & deVeau (1986) showed that use of out-patient treatment orders led to reduced readmission rates. However, these studies failed to take account of bias due to the likelihood that patients were particularly disturbed immediately before the start of the community treatment order, and thus more likely to be admitted to hospital. Bursten (1986) demonstrated a significant decrease in time spent in hospital for a group of patients following the start of a community treatment order. However, a control group of patients, not subject to compulsory community treatment, demonstrated a similar reduction of time in hospital, leading Bursten to conclude that his observed changes were most likely due to factors other than the compulsory treatment order itself.

In England and Wales there is no provision for compulsory treatment in the community under the Mental Health Act 1983, nor has there ever been such provision. However, some psychiatrists have used Section 17 of the Mental Health Act to place on leave from hospital, patients on Section 3 who require long-term maintenance treatment to prevent serious relapse, but who do not agree to comply voluntarily with necessary treatment (Rohde, 1984). In practice, this has allowed patients who stop their treatment, or whose clinical condition gives serious cause for concern, to be brought back into hospital to recommence treatment; Section 17 has not been used to enforce treatment in the community, nor has its use in this way been contemplated. In some instances, the treatment order has been renewed under Section 20. However, this use of 'extended leave' was tested in the courts in 1985 and judged illegal (*R.* v. *Gardner*, 1985; *R.* v. *Hallstrom*, 1985; Dyer, 1987).

The present study had two main aims. First, patients who had been treated with extended leave before 1986 (when this practice was still considered permissible) were compared with a control group. In particular, the study aimed to determine if the extended-leave group could be distinguished from the control group in particular characteristics which could justify the use of a community treatment order, such as a history of poor compliance with treatment, more frequent episodes of seriously dangerous behaviour, poorer social stability and more frequent and longer psychiatric admissions.

The second aim of the study was to determine if treatment with extended leave contributed to the course of the patient's psychiatric disorder in such a way as to justify its use. We hypothesised that use of extended leave would lead to improved compliance with treatment, reduced severity and frequency of episodes of dangerousness, and a reduction in frequency and duration of in-patient admissions. A number of patients were identified whose treatment with extended leave was ended not on clinical grounds but in the light of the 1985 High Court judgements (*R.* v. *Gardner*, 1985; *R.* v. *Hallstrom*, 1985). We hypothesised that ending extended leave on legal grounds in this way would reverse the likely benefits of extended leave described above.

The method used in the study was a retrospective case-note comparison. Information derived from the notes of patients treated with extended leave on Section 3 of the 1983 Mental Health Act or Section 26 of the 1959 Act was compared with data on patients of similar age, sex and diagnosis selected by consultant psychiatrists as *not* requiring compulsory treatment in the community. The latter group of patients, forming the control group, was gathered for the study described in the accompanying paper (pp. 799–804).

Method

Definitions

Extended leave (from hospital, on Section 3 – or on Section 26 of the 1959 Mental Health Act). This term is used where (a) Section 3 was extended for a further six months (under Section 20) *and* (b) the patient was not occupying a hospital bed for more than 14 days at the time of extension. The period of extended leave was measured from the date on which authority for detention was renewed (under Section 20) until the patient was discharged from Section 3.

Non-compliance with drug treatment. This means either (a) any recorded refusal to take medication, or (b) failure to take a depot injection within two weeks of the prescribed date, unless an explanation was available (e.g. physical illness necessitating admission). If non-compliance related to a single drug, and the patient was recorded as taking a substitute drug as prescribed, this was not scored as non-compliance.

Non-compliance with out-patient appointments. This means either (a) any recorded refusal to attend the out-patient clinic, or (b) failure to attend a scheduled appointment *and* not attending the subsequent or rearranged appointment without any evident explanation.

Lost to out-patient follow-up. This means failure to attend out-patient appointments for three months or longer, without being discharged from the out-patient clinic.

Dangerousness. Recorded dangerousness was assessed using ordinal rating scales (with ratings 0–4) derived from the Overt Aggression Scale (Yudofsky *et al*, 1986). Ratings were made of dangerousness to self, to other people and to objects. *Serious dangerousness* in any of these categories was defined by a score of 3 or 4. For example, for dangerousness to others, attacks which caused mild or moderate injury (bruises, sprains etc.) were rated 3 and attacks causing more severe injuries (broken bones, deep lacerations, internal injuries) were rated 4. In addition, episodes of deliberate self-harm were recorded.

Subjects and data

Patients who, before December 1985, had been treated on extended leave (forming the extended-leave group) were sought in several ways. Direct contacts were made with 26 hospitals to inquire if they had treated patients in this way. These hospitals were selected to cover a wide range of settings, from inner-city to rural, and included a wide range of different psychiatric services. Also, those attending a meeting of the Royal College of Psychiatrists on community treatment orders were canvassed to find psychiatrists who had used extended leave. In addition, the Mental Health Act Commission and the National Schizophrenia Fellowship were approached to find out if they were aware of any people treated with extended leave.

In the study described in the accompanying paper (pp. 799–804), selected consultant psychiatrists were asked to nominate patients under their care whom they would treat using a community treatment order if this were available, and to match each such patient with one or two others of similar age, sex and diagnosis for whom compulsory treatment in the community was not indicated. The latter patient group also matched the extended-leave sample in this study in terms of age, sex and diagnosis, and was therefore used as the control group. Information was gathered in the same way for both groups. However, while the researchers knew which patients belonged to the extended-leave group, they rated the patients in the accompanying study without knowing whether individual patients had been nominated for treatment with a community treatment order or as controls. In other words, the researchers collecting data were 'blind' as to which patients constituted the control group.

Information was gathered from medical case notes, admission records, Mental Health Act registers and any other documents available at the hospitals concerned. Where medical records indicated that the patient had also received treatment elsewhere, other hospitals involved were visited or contacted to gather further data.

Data collection was standardised by the use of a check-list of information required for each case. The check-list was devised in a small pilot study.

A specific 'key time' was chosen for each patient and socio-demographic data current at that time were collected. For the extended-leave patients, the key time was the date of admission as an in-patient, immediately preceding the period of extended leave. For the control group, the key time was the date of nomination, or, in the case of patients who were currently in-patients, the day prior to their admission date as in-patients. For both groups, details were collected over periods of one year and five years retrospectively from the key time. For the extended-leave group, each episode of extended leave was treated separately.

Number and duration of admissions, dangerousness, and compliance with medications and out-patient appointments were measured over the period of extended leave and a period of equal duration before extended leave. For this comparison, the extended-leave period (defined as above) was compared with a period of equal length before the admission which led directly to treatment with extended leave. Similarly, the same variables were examined for an equal time period after the extended leave period had ended.

Compliance with out-patient appointments or with medication were rated from the start of each study period on a fully anchored seven-point scale (e.g. 7 = full compliance, 3 = compliance for 3–6 months, 1 = compliance of less than 1 month). Intervals shorter than two months between successive in-patient admissions were excluded from this rating.

Analysis

Data relating to length of admissions were compared using the two-sample t-test. Comparisons between proportions were analysed using the χ^2 test, with Yates' correction where appropriate. The Komolgorov–Smirnov test was used to compare proportions of patients in the two subgroups in terms of admission frequencies (Table 2). In the mirror-image parts of the study, pair-wise comparisons were made using Wilcoxon's rank sum test or the sign test, as appropriate. The paper gives 95% confidence intervals where appropriate.

Results

The study identified 42 episodes of extended leave in 35 patients, under the care of ten consultant psychiatrists. Another six patients were identified to the researchers as having been treated with extended leave, but sufficient data could not be gathered to include them in the study. A number of other patients were said to have been treated with 'extended leave' but on closer examination of their medical records and other information it remained unclear whether they fulfilled our criteria for inclusion in the study. Of the 26 hospitals contacted direct, 19 had not used extended leave, according to the consultant psychiatrists contacted. There were 49 patients in the control group.

For both the extended-leave and control groups, all those cases in which the records permitted clinical diagnoses to be checked were of functional psychosis, predominantly schizophrenia or schizoaffective disorder.

For the extended-leave group, the mean duration of extended leave, defined as above, was 116 weeks (range 13–666 weeks). Of the 42 cases, 17 were of extended leave for one year or less, 12 for one to two years, and 13 for more than two years.

For the extended-leave patients at the key times, the mean age was 37.5 years (s.d. 8.9 years, range 19–63 years). In 24 instances of extended leave (57%) the subjects were male. In nine instances (21%) the subjects were married and in 17 (40%) they had attained an educational level beyond O level or the equivalent. There were no significant differences between the extended-leave and the control groups in any of these characteristics.

At the time of the admission leading to the period of extended leave, patients in 22 instances (52%) were living with partners or marital or natal families, and in 26 instances (62%) had lived at their current address for at least one year. The subjects of at least 28 episodes (67%) were registered with a general practitioner – this information could not be found in 26 cases. Despite the relatively high educational attainment of the extended-leave group as a whole, in only seven instances (17%) had patients been employed within one month before the admission leading to extended leave, and in 20 instances (48%) patients had been unemployed for three years or longer. Once again, no significant differences were found between the extended-leave and control groups in any of these characteristics.

For the extended-leave group, the mean duration of psychiatric illness at the time of admission leading to extended leave was 9.6 years (s.d. 8.1 years, range <1–29 years). In only 14 instances of extended leave (33%) had the patient had fewer than four psychiatric admissions preceding that leading to treatment with extended leave. In 37 instances of extended leave (88%) the patient had had previous Mental Health Act admissions. The extended-leave group had more previous compulsory admissions than the

Table 1
Dangerousness and compliance with psychiatric treatments[1]

	'Lifetime' history before 'key time'				5-year period before 'key time'				1-year period before 'key time'			
	Extended leave (42 cases)		Control (49 cases)		Extended leave (42 cases)		Control (49 cases)		Extended leave (42 cases)		Control (49 cases)	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
History of danger to self												
none serious	27	(64)	27	(55)	30	(71)	35	(71)	32	(76)	46	(93)
serious	15	(36)	22	(45)	12	(29)	12	(24)	10	(24)	3	(7)
History of danger to others												
none serious	21	(50)	35	(71)	23	(55)	38	(78)*[2]	29	(69)	45	(91)*[5]
serious	21	(50)	14	(29)	19	(45)	9	(18)	13	(31)	4	(9)
History of danger to property/ objects												
none serious	29	(69)	38	(78)	32	(76)	37	(76)	38	(90)	47	(96)
serious	13	(31)	11	(22)	10	(19)	10	(20)	4	(10)	2	(4)
History of any type of dangerousness												
none serious	11	(26)	17	(35)	24	(57)	37	(76)	28	(67)	47	(96)***[6]
serious	31	(74)	32	(65)	18	(43)	12	(24)	14	(33)	2	(4)
Compliance with out-patient appointments												
full	–		–		2	(5)	19	(39)***[3]	4	(9)	26	(53)***[7]
less than full	–		–		30	(71)	22	(45)	24	(57)	9	(18)
Compliance with medications												
full	–		–		1	(2)	7	(14)	1	(2)	11	(22)***[8]
less than full	–		–		36	(86)	25	(51)	34	(81)	15	(30)
Lost to follow-up as out-patient												
no	–		–		15	(36)	33	(67)**[4]	17	(40)	40	(82)***[9]
yes	–		–		21	(50)	9	(18)	17	(40)	1	(2)

Comparison between the two groups: $^*P<0.02$, $^{**}P<0.005$, $^{***}P<0.001$.

1. Data were unavailable in some categories for some subjects.
2. 95% CI for difference between proportions 0.08–0.46.
3. 95% CI 0.19–0.49.
4. 95% CI 0.15–0.52.
5. 95% CI 0.07–0.39.
6. 95% CI 0.14–0.45.
7. 95% CI 0.27–0.60.
8. 95% CI 0.08–0.33.
9. 95% CI 0.23–0.54.

control group: the subjects of 36% of the episodes of extended leave had had four or more Mental Health Act admissions at the key time, compared with only 14% of the controls ($\chi^2 = 9.22$; $P = 0.026$; 95% CI 0.03–0.35). In the subjects of 12 of the extended-leave episodes (29%) and in 11 of the control group (22%) there was a recorded history of criminal charges.

Clinical characteristics before extended leave

A 'lifetime' history of dangerousness was common in both groups. This was recorded in the subjects of 31 of the extended-leave episodes (74%) and in 32 of the controls (65%) (Table 1). However, the subjects of the extended-leave episodes were more likely than the controls to have a history of recent danger to others. In the five years before extended leave there were recorded episodes of serious dangerousness to others in the subjects of 19 of the extended-leave episodes (45%), compared with 9 of the control group (18%) ($P < 0.02$; 95% CI for difference between proportions, 0.08–0.46). The corresponding figures for serious dangerousness to others in the 12 months before extended leave were 13 (31%) and 4 (8%) ($P < 0.02$; 95% CI 0.07–0.39). In the 12 months before extended leave, at least one episode of serious dangerousness of some kind was recorded in the subjects of 14 instances of extended leave (33%). In the corresponding period before their nomination as controls, only 2 of the control group (4%) had shown episodes of serious dangerousness ($P < 0.001$; 95% CI 0.14–0.45). Previous drug overdoses were recorded in the subjects of 12 of the extended-leave episodes (29%), and in 16 of the controls (33%).

In the five years leading up to extended leave, the subjects of only 2 of the extended-leave episodes (5%) showed full compliance with out-patient attendance, compared with 19 of the controls (39%) ($P < 0.001$; 95% CI 0.19–0.49) (Table 1). The difference between the two groups was even more striking in the 12 months before the key time, with full compliance with out-patient attendance being shown by the subjects of 4 episodes of extended leave (9%) and 26 of the controls (53%) ($P < 0.001$; 95% CI 0.27–0.60). In 21 of the instances of extended leave (50%) the patients had been lost to follow-up at some time in the five years before the key time (Table 1). The subjects of 17 of the extended-leave episodes (40%) were lost to follow-up in the 12 months before the admission leading to extended leave, compared with only one of the controls (2%) ($P < 0.001$; 95% CI 0.23–0.54).

Over the five years before the admission leading to extended leave, in the extended-leave cases the patients had spent an average of 35 weeks in hospital, compared with 23 weeks for the control group ($P = 0.03$) (Table 2). The groups did not differ in their frequency of total admissions. However, whereas 26 (53%) of the control group had no Mental Health Act admissions in the five years preceding the key time, this was true for the patients in only 8 (19%) of the instances of extended leave ($P = 0.0002$; 95% CI for difference between proportions 0.16–0.52). A similar pattern

Table 2
Admission data for 1 year and 5 years before the 'key time'[1]

	5-year period before 'key time'		1-year period before 'key time'	
	Extended leave (42 cases)	Control (49 cases)	Extended leave (42 cases)	Control (49 cases)
Total in-patient time: weeks				
mean	35	23	8	5
standard deviation	43	24	9	9
In-patient time on Section: weeks				
mean	24	10	7	3
standard deviation	40	14	9	8
% total in-patient time on Section				
mean	62	36**[2]	51	26*[3]
standard deviation	38	38	47	41
Total in-patient admissions: patients (%)				
no admissions	1 (2)	7 (15)	11 (26)	23 (47)
1 admission	7 (17)	7 (15)	17 (40)	23 (47)
2 admissions	9 (21)	11 (23)	10 (24)	4 (8)
3–5 admissions	16 (38)	17 (34)	4 (10)	1 (2)
more than 5 admissions	9 (22)	6 (12)	0	0
Mental Health Act admissions: patients (%)				
no admission	8 (19)	26 (53)***[4]	18 (43)	41 (83)***[4]
1 admission	8 (19)	12 (24)	16 (38)	7 (15)
2 admissions	11 (26)	6 (12)	8 (19)	1 (2)
more than 2 admissions	15 (36)	3 (6)	0	0

Comparisons between the two groups: *$P < 0.02$, **$P < 0.01$, ***$P < 0.001$.
1. Data were unavailable in some categories for some subjects.
2. 95% CI for difference between means 10.1–49.8.
3. 95% CI for difference between means 6.7–43.3.
4. Kolmogorov–Smirnov test.

Table 3
In-patient admission data before and during extended leave (42 cases)

	Before extended leave	During extended leave	
In-patient admissions			
Median number of admissions	1	0	^{*1}
% cases with no admissions	24	59	
% cases with 1 admission	29	17	
% cases with 2–4 admissions	43	20	
% cases with >4 admissions	2	5	
% cases with reduced frequency of admissions during extended leave	–	56	^{**4}
% cases with increased frequency of admissions during extended leave	–	20	
Total in-patient time			
Median time as an in-patient: weeks	5	0	^{**2}
% cases with reduced in-patient time during extended leave	–	66	^{**4}
% cases with increased in-patient time during extended leave	–	20	
Duration of admissions			
Median duration of admission: weeks	3.5	0	^{**3}
% cases with decreased duration of admissions during extended leave	–	59	^{**4}
% cases with increased duration of admissions during extended leave	–	20	

$^{*}P<0.02$, $^{**}P<0.005$, $^{***}P<0.001$.
1. 95% CI for difference between medians 0.11–1.89.
2. 95% CI 4.3–5.7.
3. 95% CI 2.9–4.1.
4. Sign test.

was observed for the 12 months before the key time, although the groups differed less over this shorter interval.

Mirror-image comparisons of the extended-leave group before and during extended leave

Extended leave led to an overall reduction in number and duration of in-patient admissions, as well as the total time spent as an in-patient (Table 3). In 24 cases (56%) patients showed a reduction in number of admissions while on extended leave, while the frequency of admissions increased in 8 cases (20%). In 28 cases (67%) patients spent less time as in-patients during the extended-leave period than before it.

While incidents of serious dangerousness to others were recorded before extended leave in 24% of cases, this fell to only 5% during extended leave. Dangerousness towards others was reduced during extended leave in 22 cases (52%), and was increased in only 2 cases (5%) (sign test: $P=0.001$). Similarly, in 8 cases (19%) the patient showed a reduction in dangerousness to self while on extended leave, while there was only one case (2%) where the patient showed an increased rating of dangerousness (sign test: $P=0.02$). However, no effect was found of extended leave on recorded dangerousness towards property or objects.

Table 4
Compliance before and during extended leave (42 cases)

	Before extended leave	During extended leave
Compliance with out-patient appointments		
Median score	4	7^{***1}
% cases with full compliance	17	51
% cases with improvement during extended leave	–	43
% cases with deterioration during extended leave	–	10
Compliance with medications		
Median score	1	7^{***2}
% cases with full compliance	2	37
% cases with improvement during extended leave	–	43
% cases with deterioration during extended leave	–	10

For statistical analysis, pain-wise comparisons were made of each patient's ratings (on 0–7 scales) before and during extended leave.
$^{***}P$.
1. 95% CI for difference between medians 2.5–3.5.
2. 95% CI for difference between medians 5.5–6.5.

Extended leave had considerable effects on patients' compliance with their out-patient treatments (Table 4). During the extended-leave period, compliance improved in 18 cases (43%), and deteriorated in only 4 (10%). The percentage of cases in which patients attended all their out-patient appointments rose from 17% to 51%, and there was a parallel rise in compliance with medications.

Mirror-image comparison during and after extended leave

Particular attention was focused on those patients whose extended leave was ended within six months of the *R.* v. *Hallstrom* and *R.* v. *Gardner* judgements. In some cases, the notes recorded that the decision not to renew Section 3 was based on these court judgements rather than being taken on clinical grounds. In other instances, such a decision was not recorded but could be assumed; e.g. one patient had been treated with extended leave for several years before 1985, and no recent change in his mental state or circumstances had been recorded before the end of his period of extended leave. Thirteen patients were found whose extended leave had been discontinued in this way, on legal rather than clinical grounds.

Overall, these 13 patients had poor outcomes. Two patients committed suicide. Six have had subsequent admissions under the Mental Health Act, in one case within weeks of extended leave being ended. A further three patients from this group were lost to psychiatric follow-up after their extended leave ended (although in one case a letter in the medical records from the local housing department two years after extended leave ended suggested that he was coping adequately). One patient was immediately placed under guardianship following the end of his extended leave, and appears to have done relatively well. One patient in this group continued to comply well with medications and out-patient follow-up, and remained out of hospital after the period of extended leave.

Compared with the remainder of the extended-leave group, those whose extended leave was ended on legal grounds were significantly less likely to show good compliance with out-patient follow-up; 82% of the former group and 27% of the latter complied with their out-patient appointments for at least six months (Fisher's exact test: $P=0.012$). None of those patients whose extended leave was ended on legal grounds complied with their medications for at least six months, compared with 35% of the remainder of the extended-leave group (Fisher's exact test: $P=0.09$). However, the two groups were not significantly different in their ratings of dangerousness or in the frequency of their in-patient admissions following the end of extended leave.

Discussion

Interpretation of the results of this study must take account of its retrospective design, relying on medical records and other written information. Medical records are not always accurate and may also be incomplete. Some of the data gathered (e.g. admission and discharge dates, Mental Health Act status) were cross-checked using more than one source wherever possible. Where significant differences were found between the extended-leave group and the control patients, these differences were generally so large that only a marked systematic bias in missing data would yield a different result. For example, in Table 1, the differences in compliance between extended-leave and control groups in the 12 months before the 'key time' would become insignificant only if all the control patients with missing data were fully compliant, and none of the extended-leave patients fell into this category.

Another problem in extracting data from medical and other records is biased recording by the researchers. For the study as a whole, this was minimised by having an *a priori* set of required data, with the variables operationally defined. Initially, it was intended to collect more data than that presented. For example, an attempt was made to record a clinical profile for each case using the symptom check-list of the Present State Examination. However, this and several other variables were abandoned when a pilot study had demonstrated that the medical case notes were not of a consistently adequate standard to record them reliably.

The patients treated with extended leave all had diagnoses of psychotic disorder. Contrary to predictions from earlier research (Szmuckler *et al*, 1981), they were similar to the control patients in terms of social stability, judging by marital status, length of time in their present home, and registration with a general practitioner. The two groups were also very similar in their overall ('lifetime') forensic and psychiatric histories, including recorded episodes of dangerousness (Table 1), although the control patients were less likely than the extended-leave group to have had a previous Mental Health Act admission (Table 2). The main characteristics of the extended-leave patients which distinguished them from the control group were a history of persistently poor compliance with treatment, including out-patient attendance, and a more frequent recent history (relative to the start of extended leave) of serious dangerousness.

For the mirror-image comparison of patients before and during extended leave, the start of extended leave was taken as the date on which Section 3 was renewed under Section 20. Many of the patients treated with extended leave had already been out of hospital for some time at this point, having previously been discharged from hospital on leave under Section 17. Measuring the start of extended leave from the date on which the patient was first discharged from hospital would have been as appropriate as using the date on which Section 3 was renewed. The data were analysed using each of these dates as the start of extended leave, but only one set of results has been presented as the two methods yielded almost identical results.

In most cases, use of extended leave resulted in significant changes in the patient's state, whatever the periods before and during extended leave chosen for comparison. Extended leave reduced the total length of time spent as in-patients and also resulted in shorter admissions, although the number of admissions was not significantly altered. There was also a marked improvement in compliance, both with attendance at out-patient clinics and with medications. Some psychiatrists who used extended leave reported anecdotally that while their patients remained on Section 3 in the community, readmission was relatively straightforward, and the patients' concern to avoid this was an inducement to continue with their treatments. During extended leave also, in half the cases the patients improved in their ratings of dangerousness towards others, although extended leave appeared to have less impact on recorded danger to self and danger to objects or property.

A small subsample of the extended-leave patients, whose extended leave was definitely or probably ended on legal rather than clinical grounds, did badly on follow-up, and showed worse compliance with follow-up than the rest of the extended-leave group.

Our extended-leave patients did not constitute an exhaustive sample. No central agency keeps systematic records which would allow all patients treated with extended leave to be traced. Nevertheless, considerable efforts were made to trace patients who had been treated with extended leave, through several sources. That our extended-leave patients form a representative sample of those treated in this way is supported by the marked similarities between this sample and a group of patients selected by a different group of consultant psychiatrists as suitable for treatment using a community treatment order (see accompanying paper (pp. 799–804)). Whether or not our sample is representative, our results indicate that there is a group of psychiatric patients which benefited from treatment with extended leave.

Until its legality was tested in the courts, those psychiatrists who used extended leave employed it as a form of community treatment order. It was used to facilitate readmission to hospital of patients with a history of psychotic illness, usually with evidence of seriously dangerous behaviour, when they failed to comply with their out-patient treatment, or deteriorated clinically. It is important to reiterate that extended leave was neither used nor intended to force patients to have treatment in the community. The potential use of a community treatment order to enforce treatment in patients' own homes has aroused concern (MIND, 1987; Royal College of Nursing, undated). However, neither the Royal College of Psychiatrists (1987) nor the American Psychiatric Association (1987) have envisaged community treatment orders being used in this way. Furthermore, community treatment orders have been successfully used, as extended leave has been, without requiring this particular type of practice (Hiday & Goodman, 1982; Geller, 1986; Dedman, 1990).

Our results provide evidence that a community treatment order giving psychiatrists the power to recall patients into hospital might be expected to benefit a small group of patients with severe mental illness in improving their compliance as out-patients and reducing the time they spend in hospital, particularly under Section. Without the possibility of compulsory out-patient treatment, the results confirm that this group of patients is likely to fare badly, particularly in terms of remaining in the community.

Acknowledgements, references and author details are given at the end of the accompanying paper (pp. 799–804).

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Compulsory Psychiatric Treatment in the Community
II. A Controlled Study of Patients whom Psychiatrists would Recommend for Compulsory Treatment in the Community

TOM SENSKY, TIMOTHY HUGHES and STEVEN HIRSCH

Several English consultant psychiatrists were asked to identify which patients currently under their care they would recommend for treatment with a community treatment order, if such a provision existed. The psychiatrists were asked to match each such 'nominated' patient for age, sex and diagnosis with one or two control patients, not considered to require compulsory treatment in the community. From specific data collected, it was found that: the two groups did not differ in their 'lifetime' histories of psychiatric admissions, substance misuse, criminal charges or dangerousness; 65–72% of the total sample had a history of serious dangerousness; but in the 12 months before nomination, the 'nominated' patients were significantly less likely than the controls to have complied with psychiatric treatment, and more likely to have defaulted from follow-up. The results indicate that a psychiatrist's decision to recommend a patient for treatment with a community treatment order will depend predominantly on specific criteria related to the patient's recent past.

There is no therapeutic option available for a small group of patients who remain well out of hospital as long as they comply with their treatment regimes but commonly require compulsory admission to hospital when they relapse. This has fuelled the debate on the need for new legislation to cover community treatment. Additional momentum for such legislation comes from the currently growing emphasis on community care and the related pressure on mental health services to reduce their reliance on in-patient facilities. Patients treated with 'extended leave' from hospital under Section 3 probably resemble closely those who would be recommended for treatment using a community treatment order. Use of extended leave led to improvements in patients' compliance with psychiatric treatment, and reduced time in hospital and less dangerous behaviour (see accompanying paper (pp. 792–799)). This indicates that a community treatment order is likely to be effective, at least in some instances. However, not all psychiatrists used extended leave before its use was judged illegal. Hence it is unclear whether the same criteria which determined the use of extended leave (see accompanying paper) would also apply to psychiatrists' recommendations for treatment using a community treatment order, if such an order existed.

Key aspects of the matter are whether or not psychiatrists would use specific criteria to determine the need for compulsory community treatment, and whether or not such criteria would be consistently applied. Extending compulsory psychiatric treatment into the community would have widespread implications for the legal rights of individual patients. It would be impossible to justify such a step if psychiatrists, as those who would be involved in making the medical recommendations for such community treatment, differed widely in the criteria determining their recommendations. Conversely, the demonstration that psychiatrists consistently used a limited set of specific criteria in recommending compulsory community treatment would provide support for the introduction of a community treatment order.

Available data, predominantly from the USA, do not provide an answer to this question, for two main reasons. Firstly, there is no applicable Federal statute and the relevant laws differ from one state to another (American Psychiatric Association, 1987; Monahan & Shah, 1989). Thus data from different states are difficult to compare. Secondly, decisions regarding commitment to compulsory psychiatric treatment, whether in the community or as an in-patient, commonly rely more on the courts and less on the direct judgement of mental health professionals than is the case in the UK.

The present study therefore aimed to examine the validity of English psychiatrists' judgements of the need for compulsory community treatment. A number of consultant psychiatrists were asked to nominate patients from among those they were currently treating who, in the psychiatrist's opinion, would be suitable for treatment with a community treatment order (based on the form of order suggested by the Royal College of Psychiatrists). These patients (the 'nominated' group) were compared in terms of their clinical and social characteristics with a control group of patients, under the care of the same consultants and matched with the nominated patients for age, sex and diagnosis. The patient variables assessed were identical to those in the accompanying study of patients who had been treated in the community on extended leave under Section 3 before this practice was judged illegal in late 1985 (see accompanying paper (pp. 792–799)). It was hypothesised that patients recommended for compulsory treatment in the community would have a history of serious mental illness and would show significantly worse compliance with their out-patient treatments (leading to relapse and hospital admission) than a control group of patients, matched for age, sex and diagnosis but considered not to require treatment with a community treatment order. In addition, it was considered likely that these patients nominated for compulsory community treatment would have a history of dangerousness on relapse.

Method

Non-compliance, loss to out-patient psychiatric follow-up, and dangerousness were operationally defined as described in the accompanying paper (pp. 792–799).

A number of consultant psychiatrists in London and the Home Counties were asked to identify patients currently under their care whom they would wish to treat using a community treatment order were such an order available. The form of the order was taken from that recommended by the Royal College of Psychiatrists (equivalent to Section 3, but not requiring in-patient detention). For each such nominated patient, the psychiatrist was asked to provide the names of one or two control patients, matched for age, sex and diagnosis with the nominated patient but not considered suitable for treatment with a community treatment order. With two exceptions, none of the psychiatrists who nominated patients for this study had previously used extended leave under Section 3 (or Section 26 of the 1959 Act) to manage patients in the community.

Data were collected as described in the accompanying paper (pp. 792–799). Relevant variables were decided before the start of data collection; a check-list was devised, and tested in an initial pilot study. To reduce possible bias in data collection and recording, the research workers collecting data were not aware which patients had been nominated for compulsory community treatment and which were controls. For each patient the 'key time' for data was taken as the date of nomination, or in the case of patients in hospital at the time of nomination, the key time was taken as the day prior to their admission. Sociodemographic data current at the key time were collected, as were clinical and

Table 1
Psychiatric and forensic histories[1]

	Nominated group ($n = 29$)		Control group ($n = 49$)	
	No.	(%)	No.	(%)
Total psychiatric admissions				
less than 4	6	(21)	12	(24)
4–9	10	(34)	16	(33)
10 or more	11	(38)	15	(30)
Mental Health Act admissions				
none	4	(13)	15	(30)
1–3	20	(69)	27	(55)
4–6	3	(10)	4	(8)
7 or more	2	(7)	3	(6)
Section 136 admissions				
none	15	(52)	27	(47)
one	3	(10)	18	(37)
more than one	11	(38)	7	(14)
Recorded history of drug abuse				
yes	10	(34)	10	(20)
no	19	(66)	39	(80)
Recorded history of alcohol abuse				
yes	9	(31)	9	(18)
no	20	(69)	40	(82)
Recorded criminal charges				
none	15	(52)	38	(78)
one	7	(24)	3	(6)
more than one	7	(24)	8	(16)

None of the differences between the groups is statistically significant.

1. Data were unavailable in some categories for some subjects.

other details over periods of one year and five years retrospectively from the key time. Compliance with out-patient appointments and with medication were rated as described in the accompanying paper.

Analysis

Admission data were compared using the two-sample t-test. Frequency data were analysed using the χ^2 test, with Yates' correction where appropriate. Where appropriate, 95% confidence intervals were calculated for the difference between means or proportions. Frequencies of admissions (i.e. nominal data arranged in rank order) were compared in the two groups using the Komolgorov–Smirnov test.

Results

There were 34 patients nominated as suitable for treatment using a community treatment order, by a total of ten consultant psychiatrists. Data adequate for analysis could be collected on 29 of these. Only two of the psychiatrists who nominated patients for this part of the study had previously treated patients with extended leave. There were 49 control patients.

All those cases in which the records permitted clinical diagnoses to be checked showed substantial evidence of functional psychosis, predominantly schizophrenia or schizoaffective disorder.

The nominated patients had a mean age of 37 years (s.d. 9.4, range 22–62). The mean age of the control patients was 39.9 years (s.d. 11.7, range 23–74). In the nominated group 16 patients (55%) were female and in the control group 24 (49%). There were 23 single patients in the nominated group (79%), compared with 24 in the control group (49%) ($\chi^2 = 5.36$; $P = 0.02$; 95% CI for difference between proportions, 0.09–0.50). There were 18 nominated patients (62%) and 21 control patients (43%) living alone (NS). In the nominated group, 14 patients (48%), and in the control group 15 patients (31%), had changed their home address at least once in the three years before the key time. None of the nominated patients were employed at the key time, and the most of the patients in both groups had been unemployed for three years or more (72% of the nominated group and 63% of the controls). Patients registered with a general practitioner comprised 92% of the whole sample; there was no difference between the two groups in this respect.

The two groups were very similar in their 'lifetime' histories of criminal charges and substance misuse (Table 1). The groups also did not differ significantly in their total number of psychiatric admissions and admissions under the Mental Health Act (Table 1). However, over the five-year period before the key time, the nominated group spent longer as psychiatric in-patients, particularly under the Mental Health Act, and had more frequent Mental Health Act admissions than the control group (Table 2).

The two patient groups were not significantly different in their 'lifetime' histories of dangerousness, except that the nominated patients more frequently had a history of serious dangerousness to objects or property (Table 3). There was a history of some form of serious dangerousness for 72% of the nominated patients and 65% of the control group.

In the five years preceding the key time, the two groups were virtually indistinguishable in terms of dangerousness and in terms of compliance with psychiatric treatments (Table 3). However, in the 12 months before the key time, the nominated patients were significantly less compliant with their psychiatric treatment than the controls, and were also more likely to default from out-patient follow-up. Only one patient in the nominated group complied fully with his medications in the 12 months before the key time, and 18 (62%) were lost to follow-up for three months or longer.

The patients selected for treatment with a compulsory community order in this study resembled very closely the sample of patients described in the accompanying study, treated using extended leave on either Section 3 of the current Mental Health Act or Section 26 of the 1959 Act (see accompanying paper). When compared on each of the variables assessed in the two studies, only two statistically significant differences emerged. Compared with extended-leave patients, the nominated group were more likely to be living alone ($\chi^2 = 15.35$; $P < 0.001$) and to have changed addresses within the previous three years ($\chi^2 = 7.34$; $P < 0.01$).

Table 2
Admission data for 1 year and 5 years before 'key time'[1]

	5-year period before 'key time'		1-year period before 'key time'	
	Nominated group ($n=29$)	Control group ($n=49$)	Nominated group ($n=29$)	Control group ($n=49$)
Total in-patient time: weeks				
mean	39	23^{*2}	15	5^{**4}
standard deviation	29	24	15	9
In-patient time on Section: weeks				
mean	24	10^{**3}	9	3^{*5}
standard deviation	20	14	11	8
Total in-patient admissions: patients (%)				
no admissions	1 (3)	7 (15)	7 (24)	23 (47)
one admission	4 (14)	7 (15)	10 (34)	23 (47)
two admissions	5 (17)	11 (23)	7 (24)	4 (8)
3–5 admissions	11 (38)	17 (34)	5 (17)	1 (2)
more than 5 admissions	8 (28)	6 (12)	0	0
Mental Health Act admissions: patients (%)				
no admissions	3 (10)	26 $(53)^{***6}$	17 (59)	41 $(83)^{**7}$
one admission	7 (24)	12 (24)	7 (24)	7 (15)
two admissions	9 (31)	6 (12)	5 (17)	1 (2)
more than 2 admissions	10 (34)	3 (6)	0	0

Comparisons between the two groups: $^*P<0.02$, $^{**}P<0.01$, $^{***}P<0.001$.

1. Data were unavailable in some categories for some subjects.
2. 95% CI for difference between means 3.9–28.1.
3. 95% CI 6.3–21.7.
4. 95% CI 4.6–15.4.
5. 95% CI 1.7–10.3.
6. $\chi^2=20.83$, $P<0.001$; Komolgorov–Smirnov test $P<0.001$.
7. $\chi^2=8.00$, $P=0.01$; Komolgorov–Smirnov test NS.

Discussion

This study represents the first attempt to determine the basis on which consultant psychiatrists in England would recommend the use of a community treatment order, if one existed. The sample of consultant psychiatrists who participated in this study was small, but their practices covered a variety of catchment areas, ranging from inner-city to rural. However, it is not possible to determine how representative these consultants are of all those in England and Wales. Nevertheless, the results of this study at least demonstrate the possible or potential use of a community treatment order.

The psychiatrists who nominated cases were not given precise instructions about the detailed form of the community treatment order. This was deliberate: it was considered inappropriate to impose such details on the instructions given to the consultants, given that no community treatment order currently exists in England and Wales. Feedback from the consultants involved indicated that they had considered the community order to operate in the same way as extended leave from hospital under Section 3: that the order would not impose treatment on the individual in his/her own home or in the community, but would, for example, allow re-admission to hospital when the patient declined treatment. In this context, it is significant that there were striking similarities between the nominated patients and the sample of patients previously treated (by different psychiatrists) with extended leave.

Use of a community treatment order would clearly involve others, notably relatives, approved social workers, general practitioners and community psychiatric nurses. No attempt was made in the present study to examine the roles of these other people. The data cannot therefore be taken to reflect likely practice, beyond that of the psychiatrists, which formed the exclusive focus of this study.

Overall, there were only subtle differences between those patients nominated for treatment using a community treatment order and the control patients. This makes it unlikely that data collection was subject to bias, remembering that the researchers who collected the data were unaware to which category individual patients had been assigned.

Nominated patients had a background of less social stability than either the control patients or those in a sample of patients treated with extended

Table 3
Dangerousness and compliance with psychiatric treatments[1]

	'Lifetime' history before 'key time'				5-year period before 'key time'				1-year period before 'key time'			
	Nominated group (n = 29)		Control group (n = 49)		Nominated group (n = 29)		Control group (n = 49)		Nominated group (n = 29)		Control group (n = 49)	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
History of danger to self												
none serious	17	(59)	27	(55)	20	(69)	35	(71)	23	(80)	46	(93)
serious	12	(41)	22	(45)	9	(31)	12	(24)	6	(20)	3	(7)
History of danger to others												
none serious	20	(69)	35	(71)	20	(69)	38	(78)	26	(90)	45	(91)
serious	9	(31)	14	(29)	8	(28)	9	(18)	3	(10)	4	(9)
History of danger to property/objects												
none serious	13	(45)	38	(78)**[2]	19	(66)	37	(76)	24	(83)	47	(98)
serious	16	(55)	11	(22)	10	(34)	10	(20)	5	(17)	2	(4)
History of any type of dangerousness												
none serious	8	(21)	17	(35)	18	(62)	37	(76)	24	(83)	47	(96)*[3]
serious	21	(72)	32	(65)	11	(38)	12	(24)	5	(17)	2	(4)
Compliance with out-patient appointments												
full	–		–		3	(10)	19	(39)	4	(13)	26	(53)**[4]
less than full	–		–		18	(62)	22	(45)	13	(45)	9	(18)
Compliance with medications												
full	–		–		1	(3)	7	(14)	1	(3)	11	(22)***[5]
less than full	–		–		27	(93)	25	(51)	22	(76)	15	(30)
Lost to follow-up as out-patient												
no	–		–		15	(51)	33	(67)	18	(62)	40	(82)***[6]
yes	–		–		13	(45)	9	(18)	9	(31)	1	(2)

Comparisons between two groups: *$P<0.02$, **$P<0.005$, ***$P<0.001$.

1. Data were unavailable for some patients in some categories.
2. 95% CI for difference between proportions 0.11–0.54.
3. 95% CI 0.02–0.28.
4. 95% CI 0.21–0.58.
5. 95% CI 0.06–0.32.
6. 95% CI 0.11–0.46.

leave (see accompanying paper (pp. 792–799)): they were more likely to be living away from their families and to have changed addresses in the recent past. In the 12 months before the time of nomination for compulsory community treatment, the main difference between the nominated patients and the control group was the former group's poor compliance with treatment. This appears to be the key feature in the decision to commit the patient to compulsory community treatment. Thus the characteristic profile which emerges of the patients likely to be recommended by consultant psychiatrists for compulsory community treatment is of a history of functional psychosis, numerous admissions to hospital (some under the Mental Health Act), a 'lifetime' history of serious dangerousness, and a recent history of poor compliance with treatment and with out-patient follow-up.

These results suggest that the decision to treat a patient with extended leave is unlikely to be based on a global assessment of the patient's past history or mental state, but will depend predominantly on a small number of selected criteria relating to the patient's recent past. The same criteria emerged in this study as applied to the previous use of extended leave (see accompanying paper). Taken together, the studies show encouraging evidence that psychiatrists would use a community treatment order selectively, if one existed, and that its use would be potentially beneficial to the patients thus treated.

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Day Care in an Inner City
I. Characteristics of Attenders

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The socio-demographic and clinical characteristics of patients attending psychiatric day care in an inner-urban catchment area were assessed using structured techniques. The overall prevalence of the use of day care was high (164 per 100 000 total population), and 86% of attenders were in prolonged psychiatric contact. Of those in prolonged contact, the clinical and social morbidity of 68 attenders at National Health Service day hospitals was strikingly similar to that of 42 attenders at other units. Users of a 'community mental health centre' and two work centres were less disabled than attenders at other day units. Implications of these results for the organisation of day services and training of staff are discussed.

Day care forms a vital component of the contemporary community-orientated psychiatric service. However, there is considerable confusion among planners and practitioners about what it actually is, what its legitimate functions are and how these functions may best be carried out (Holloway, 1988*a*). This paper presents the results of detailed clinical and social assessment of the chronically mentally ill day-care attenders living in the inner-city catchment area of a teaching hospital's department of psychological medicine. A companion paper (pp. 810–816) presents an evaluation of the day units serving the area using the 'needs-assessment' technique developed by the Medical Research Council Social Psychiatry Research Unit (Brewin *et al*, 1987). Users' views of their care, an evaluation of the drug treatment provided to attenders and a normalisation-based evaluation of the service have been reported previously (Wainwright *et al*, 1988; Holloway, 1988*b*, 1989).

The catchment area within which the study was carried out forms part of the sixth most socially deprived health district in England and Wales according to the Jarman indices (Jarman, 1981). The district's social deprivation is reflected in heavy use of all forms of medical care (Golding *et al*, 1986), including in-patient psychiatric care (Holloway *et al*, 1988). At the time of the study, formal psychiatric day care was provided in six settings. These were a purpose-built day hospital (day hospital A); three day centres run by the local authority social service department (day centres A, B and C); a work centre for the handicapped run by a voluntary agency; and the rehabilitation day hospital serving the other sector of the district (day hospital B). People disabled by mental illness could also attend the local Remploy factory. The local-authority day centres each served a part of day hospital A's catchment area together with a part of an adjacent health district. The work centre served and was funded by three London boroughs.

A census was taken of all users of these psychiatric day units who lived in the catchment area. Attendance was defined as use of the facility on one occasion within the previous month. Day services for the elderly mentally ill and the mentally handicapped were not surveyed. Patients under 18 years of age and those over 65 with a primary diagnosis of dementia were excluded from the survey.

Attenders were divided into two groups, those who had been in continuous contact with psychiatric services of any kind for a year or more without a break of more than three months, and those whose continuous contact was less than a year. In all, 133 attenders were identified, of whom 115 were in 'prolonged psychiatric contact' (86%) and 18 were in 'brief contact'. The proportion of prolonged-contact attenders in day hospitals (87%) was very similar to the proportion in other settings (85%). This paper presents data collected on the 110 prolonged-contact attenders who agreed to be included (the 'prolonged-contact sample').

The estimated population of the catchment area was 81 000 in 1984, representing an overall rate of use of psychiatric day care of 164 per 100 000 total population. This figure does not readily translate into a number of 'day places' used by the local population, since most of the units allowed or even encouraged users to attend less than a full week. Day hospitals were used by 98 per 100 000 (60%) and other facilities by 67 per 100 000 (40%). This excludes the day-activity services provided within hospitals for in-patients and what little psychogeriatric day care was available within the catchment area.

Method

Data were collected on the sociodemographic background, history of contact with psychiatric services, social functioning, social skills, material conditions, and clinical and behavioural problems of attenders. Attenders who agreed to participate in the study were interviewed and a member of staff who knew the attender well was asked to fill in a series of questionnaires. The staff informant was subsequently interviewed to confirm that problems identified at interview and from the questionnaires remained active. Where possible, background and historical data were corroborated using the medical case notes.

A Social Performance Interview (SPI) was carried out. This provided ratings of the performance by the respondent within the past month in 12 significant areas of social functioning: personal hygiene, shopping, cooking, household chores, managing money, child care, use of public transport, use of public amenities, leisure activities, literacy, numeracy, and decision-making. The rating scale and a sample item are shown in Appendix 1. A rating manual was produced giving examples of ratings of each item.

The item scores on the SPI were used to calculate overall social performance scores. The coefficient α (Cronbach, 1951) for item scores of the SPI schedule was 0.71, indicating that the items are of adequate internal consistency, and providing justification for summing scores across items. The inter-rater reliability of the SPI was assessed by obtaining independent ratings from a series of audio-taped interviews which had been transcribed. Item reliabilities were high, with weighted κ values (Cichetti, 1976) falling below 0.79 for only two items (weighted κ 0.51 for cooking, 0.43 for leisure activities). The intercorrelation between overall social performance scores obtained during the inter-rater reliability study was high ($r=0.93$, $P<0.0001$). The social performance scores are used as a measure of overall social morbidity in this paper.

A staff-rated Social Performance Questionnaire (SPQ) was also obtained, covering the same 12 items as the SPI. An example of an SPQ item is shown in Appendix 2. The coefficient α for the SPQ was 0.72. The inter-informant reliability of the SPQ was assessed by obtaining ratings on 17 attenders at day hospital A. The social performance total scores correlated highly ($r=0.90$, $P<0.001$); individual item reliability was also reasonably satisfactory, weighted κ being under 0.7 for only four items. The Pearson correlation coefficient between the SPI scores and the SPQ scores for the whole sample was 0.72 ($P<0.0001$), giving some support to the validity of these two independent measures of social disability.

Information from the SPI and SPQ was combined to provide an overall rating of functioning in 11 areas (literacy and numeracy forming a single item), and the existence of a clinically significant problem in functioning in an area was confirmed at interview with a key staff informant. Out of 150 problems in social functioning identified in the cases where both SPI and SPQ data were available, 52 were rated in the SPI alone, 74 in both schedules, 18 in the SPQ alone and 6 from other sources.

Three social-skills items (non-verbal communication, conversation and social mixing, and initiation of conversation) were rated on a three-point scale at interview with the attender, and by a staff informant in a questionnaire. Social skills scores were calculated from the interview and questionnaire. Correlation between the two scores was significant but not high (Pearson correlation coefficient $r=0.56$, $P<0.0001$). Agreement between staff raters was higher ($r=0.64$, $P<0.0001$). Data from both sources were combined to provide a global rating of social-skills problems.

The financial and housing situations of attenders were assessed at interview: a significant problem was rated as present if the respondent reported damp, overcrowded or noisy housing, homelessness, debt, or inadequate money for food. The welfare benefits received by attenders were recorded.

Assessment of clinical state and behavioural problems

The case-note psychiatric diagnosis of attenders was recorded, and a study diagnosis was made following the full assessment procedure. Case-note and study diagnoses differed in 13 of the 89 attenders on whom psychiatric case notes were available.

Eleven clinical and behavioural problems were assessed: delusions/hallucinations, depression, anxiety symptoms, poor concentration/memory impairment, drug/alcohol abuse, side-effects of medication, physical illness, slowness/underactivity, socially embarrassing behaviour, aggression, and psychosocial distress.

Current mental state was assessed using the development version of the Present State Examination 10th edition (PSE-10; Brugha *et al*, 1988). The author received training in the use of the instrument and participated in assessing its reliability. PSE-10 requires a rating of concentration and includes the Mini Mental State Examination (Folstein *et al*, 1975). The reported consumption of drugs and alcohol was noted and the CAGE questionnaire (Ewing, 1984) was administered. Two measures of side-effects were carried out, the TAKE examination (Wojcik *et al*, 1980) and the Abbreviated Tardive Dyskinesia Scale (Simpson *et al*, 1979). Attenders were asked to report significant physical illness. The behavioural problems slowness/underactivity, socially embarrassing behaviour and aggression were rated within the PSE. Psychosocial distress (i.e. severe worry about personal relationships, housing and financial conditions) was rated during an interview investigating the respondent's personal circumstances. Additional information in each problem area was obtained from a questionnaire filled in by staff, and the current existence of an active problem was confirmed at interview with a staff informant.

Results

For the sample as a whole the numbers of men and women were almost equal (48% male, 52% female), although eight of the ten patients attending units offering sheltered work were men. The mean age was 46 years, with a range of 20–80 years. All ten attenders aged over 65 years attended day hospital A. Six of these had begun attending before the age of 65. The proportion of attenders from ethnic minority groups (24%) was identical to the overall proportion within the catchment area (Lambeth Council, 1981). However, 64% of the under-30s in the sample were from ethnic minorities; a similar finding has been reported in the in-patient unit serving the catchment area (Patrick *et al*, 1989).

Exactly half the sample were single, 18% were married or cohabiting, and 32% were separated, widowed or divorced. Nearly half of the sample (48%) lived with a relative, either a spouse (18%), parents (17%) or some other relative (13%). (The last figure includes two attenders who were living with dependent children as a single-parent family, as well as patients living with siblings or other kin.) Just over a third of the sample (35%) lived independently in a flat or house. Of the 19 attenders (17% of the sample) living in some form of residential provision, only eight were in facilities used exclusively by the mentally ill. The other 11 were in facilities used by a variety of single, homeless persons. This reflects the dearth of specialised accommodation within the district, particularly of an intensively staffed nature.

The three Remploy workers and one patient attending day hospital B were receiving payment for their work, and could be said to be in regular employment at the time of the census. One other attender had a part-time job in addition to attending a day unit. Of the other 105 attenders, only five had worked in the past year, while 74 had not worked in the last five years. All those not working received benefits from the state.

Personal hygiene was significantly poor in 12% of the sample. Daily living skills such as shopping (24%), cooking (25%), household chores (32%), managing money (21%) and use of public transport (18%) were commonly impaired. More day-hospital patients were rated as experiencing a problem in using public transport than attenders at other units (17 out of 68 compared with 3 out of 42: $\chi^2=5.56$, 1 d.f., $P<0.02$). This reflects the insistence of other day units that attenders be able to make their own way to their unit. There were no other significant differences in social functioning between day-hospital and other attenders. However, attenders at day centre B (the 'community mental health centre') had significantly lower total SPI scores than attenders at the other two main day units serving the catchment area. Mean SPI scores for each unit in the study are presented in Table 1.

A social-skills problem was rated as present in 30% of the sample. No attender at day centre B, the work centre or the Remploy factory had severely impaired social skills, while a social-skills problem was rated in 41% of attenders at day centre A and 36% of attenders at day hospital A. The difference between day centre B and day hospital A was significant ($\chi^2=7.4$, 1 d.f., $P<0.01$), as was the difference between centres A and B ($\chi^2=6.6$, 1 d.f., $P<0.01$). A severe housing or financial problem was rated in 18% of the sample. There was no evidence of a difference between day-hospital attenders and those attending other units.

Clinical characteristics of prolonged-contact attenders

Clinical characteristics of the sample are summarised in Table 2. Just under half of the sample received a diagnosis of schizophrenia, schizoaffective psychosis or paranoid psychosis. Schizophrenia was the commonest diagnosis in all settings except day centre B, where the majority of attenders suffered from neurotic problems or alcohol abuse.

Most patients in the sample had substantial psychiatric histories. The mean length of time since first psychiatric contact, generally an episode leading to in-patient admission, was 15.0 years. Only ten attenders had never been in-patients. The mean number of previous admissions reported by patients was 3.7, with 44 patients reporting being admitted five or more times. (Attempts were made to verify the patients' reports from case-notes, but psychiatric case-notes were not always available for the patients not attending hospitals.) The day-hospital attenders had on average been admitted more often than attenders at the other units (mean number of admissions for day hospital patients = 4.2, for attenders at other units = 3.0: ANOVA, $F=5.88$, 1 d.f., $P<0.02$). Fifteen attenders, although in continuous psychiatric contact, had been in their day unit for less than a year. The mean length of current stay was 3.1 years. Twenty-four patients had been continuously attending their day unit for more than 5 years. There was no difference in average length of stay between day-hospital attenders and those attending other units.

Schizophrenia was diagnosed in 17 of the 26 Afro-Caribbean and Asian attenders, compared with 36 of the other 84 attenders ($\chi^2=4.03$, 1 d.f., $P<0.05$). Of the 53 attenders with a diagnosis of schizophrenia, 35 were men ($\chi^2=11.8$, 1 d.f., $P<0.01$). (Conversely, only 3 of the 15

Table 1
Social Performance Interview scores and clinical and behavioural problems of 110 prolonged-contact attenders

	Day hospital A ($n=64$)	Day hospital B ($n=4$)	Day centre A ($n=17$)	Day centre B ($n=13$)	Day centre C ($n=6$)	Work centre ($n=3$)	Remploy factory ($n=3$)
Social Performance Interview Score	4.95[1]	5.50	5.62[2]	2.46[1,2]	6.00	3.00	2.66
Mean number of clinical and behavioural problems	3.7[3]	3.8	4.2	2.9	2.0	3.3	1.0

1. Difference between day hospital A and day centre B: *t*-test, $t=2.81$, $P<0.01$.
2. Difference between day centre A and day centre B: *t*-test, $t=2.64$, $P<0.02$.
3. ANOVA, $F=2.2$, 6 d.f., $P<0.05$.

Table 2
Clinical characteristics and previous service use of 110 prolonged-contact attenders

	Day hospital A ($n=64$)	Day hospital B ($n=4$)	Day centre A ($n=17$)	Day centre B ($n=13$)	Day centre C ($n=6$)	Work centre ($n=3$)	Remploy factory ($n=3$)
Age: years							
mean[1]	47.2	56.0	45.1	41.4	40.5	28.7	51.0
range	20–80	40–64	27–60	22–52	26–64	27–29	34–63
Diagnosis							
% schizophrenia	47	75	47	23	50	100	100
% affective psychosis	19	–	6	8	17	–	–
% neurosis	20	25	12	38	17	–	–
% other	14	–	35	33	17	–	–
Previous psychiatric admissions[2]	4.2	5.0	3.6	3.0	1.7	1.3	4.3
Past psychiatric history:[3] years	14.5	30.5	15.4	13.0	11.8	5.7	27.0
Years in unit[4]	2.9	6.7	3.0	2.6	3.2	1.3	5.0
Age at first psychiatric contact	32.8	25.5	29.7	28.4	28.2	23.0	24.0
Attenders seeing psychiatrist							
number	64	4	10	5	3	3	1
(%)	(100)	(100)	(58)	(38)	(50)	(100)	(33)

1. Differences between all day units: ANOVA, $F=1.60$, 6 d.f., $P=0.15$, NS.
2. Differences between all day units: ANOVA, $F=1.84$, 6 d.f., $P=0.10$, NS.
3. Differences between all day units: ANOVA, $F=3.19$, 6 d.f., $P<0.01$.
4. Differences between all day units: ANOVA, $F=2.66$, 6 d.f., $P<0.02$.

patients with a diagnosis of manic–depressive illness were men.) Similar results were found in a survey of prolonged-contact users of day care from Camberwell (Wing, 1982), and ethnic differences in diagnostic composition have been reported in case-register studies, local surveys and national studies of admission patterns (Bebbington *et al*, 1981; Dean *et al*, 1981; Patrick *et al*, 1989).

A rating of clinical depression was given for 38% of attenders, while 34% exhibited specific neurotic symptoms such as anxiety. Significant physical illnesses were common (36% of the sample), as were side-effects of medication (30%), poor concentration (52%) and psychosocial distress (75%). Socially embarrassing behaviour was rated as a problem in 23%, slowness and underactivity in 18% and aggression in only 7% of the sample. There were few differences between day-hospital patients and attenders at the other units. Clinically, significant depression was more common among day-hospital patients, being rated in 31 out of 68, compared with 11 cases out of 42 in the other units ($\chi^2=4.14$, 1 d.f., $P<0.05$).

The drinking behaviour of attenders at day centre B was very different from that of the sample as a whole, with 11 out of 13 attenders admitting to consuming alcohol in the previous month, compared with only 40 of the other 96 attenders rated on this item. A striking number of attenders at day centre B had drug or alcohol problems: 6 out of 13, compared with a total of 10 of the 96 attenders at the other settings. The three Remploy workers lacked psychiatric problems, although two suffered from side-effects of their medication and one was physically ill.

The mean number of clinical and behavioural problems for the sample as a whole was 3.6: day-hospital attenders had a mean score of 3.8, compared with 3.2 for attenders at other units (ANOVA; $F=1.96$, 1 d.f., $P<0.2$, NS). The mean scores of attenders at each unit are shown in Table 1. There were significant differences between units, with the highest mean scores at day centre A and the two day hospitals.

Discussion

This cross-sectional survey inevitably fails to provide a full picture of the dynamics of the use of psychiatric day care within the catchment area. However, throughput of attenders within the local day-care system is slow. One year after the census, 75% of both the prolonged-contact and brief-contact samples were still attending their day unit. The apt metaphor of a 'stage army' has already been applied to a population in contact with a day-care service (Pryce, 1982). The relatively enduring nature of disability among prolonged-contact day patients has been documented (McCreadie *et al*, 1988).

Day hospitals offered places to more attenders than social service department and voluntary sector day centres and a largely long-term rather than acute service. Other studies have reported similar findings (Wykes *et al*, 1982; Pryce *et al*, 1983; McCreadie *et al*, 1984; Brewin *et al*, 1988). There is evidence that in many areas the day-care system envisaged in the Government White Paper *Better Services for the*

Mentally Ill (Department of Health and Social Security, 1975), in which 'acute' day care would be provided by the National Health Service, with longer-term 'social' day care being provided by local-authority day centres, has not developed.

The differing assessment methods and inclusion criteria of the epidemiologically-based studies of day care that have been carried out in Britain (Wing, 1982; Pryce *et al*, 1983; Brugha *et al*, 1988) make comparison between studies difficult. There is, however, an enormous range in utilisation of day services, from 31 per 100 000 in Scotland (McCreadie *et al*, 1984) to 164 per 100 000 in the present study. This range must reflect both variations in the levels of provision and the association between service use and socio-economic deprivation (Hirsch, 1988).

The finding that, on average, day-centre clients were as disabled as, or even more disabled than, those who attended day hospitals has also been previously reported (Wykes *et al*, 1982; Brewin *et al*, 1988). Wykes *et al* (1982) noted that although average levels of disability were similar, the day hospitals in their study accepted patients with more problems than the other units, and therefore the most disabled attenders were in the day hospitals. There was no evidence that this was the case in present study. The needs for treatment and care of prolonged-contact users in the two service systems appeared very similar. The logic of a jointly managed, integrated day service seems overwhelming; the barriers to such a development are formidable (Audit Commission, 1986), but not insurmountable, given sufficient will at a senior level (Vaughan, 1986).

The low level of psychiatric disability encountered at one of the day centres (centre B, the 'community mental health centre') deserves comment. This unit was the only source of local-authority day care to a proportion of the catchment area. The philosophy of the unit, whose staff rejected concepts of mental illness and concentrated on providing a "flexible and responsive environment to anyone in the community who considers himself to have a mental health problem", differed from the more pragmatic approach of other units. It may be that the drop-in service offered produced a social environment within which more socially disabled people felt uncomfortable and consequently stopped attending (Bender & Pilling, 1985). There is a continual danger for services for the mentally ill to move away from providing for those with long-term and apparently intractable problems, to more fashionable and apparently therapeutic activities with the less disabled.

It has for many years been Government policy that local-authority social service departments play the leading role in the provision of community care. This has been given new impetus with the publication of the White Paper *Caring for People* (Her Majesty's Stationary Office, 1989). The implications for the transfer of responsibility for the prolonged-contact day-care users identified in this study are potentially very alarming. A substantial transfer of material resources from the National Health Service would have to occur (without any guarantee that these resources would continue to be allocated for the mentally ill). In addition, day-centre workers will require skills of assessment and treatment of the manifold needs of the mentally ill. Staff will also need an understanding of the issues involved in maintaining a rehabilitative environment that fosters increased independence of users (Lavender & Sperlinger, 1988).

The degree of psychiatric morbidity experienced by day-care users has clear implications for the training needs of staff. The nature of that morbidity, comprising clinical and behavioural problems, impairments of social functioning and individual and societal reactions to mental illness (Wing, 1972), calls into question the division between 'medical' and 'social' care that lies at the heart of the proposed structure of services for community care set out in *Caring for People* (Holloway, 1990).

Appendix 1: SPI rating scale and sample item

Social Performance Interview rating scale

NB Rating performance in past month

0 = No difficulties in area, or minor difficulties without significant restriction of function.
1 = Significant restriction of function and/or extra help required for adequate performance.
2 = Marked restriction in function and/or considerable degree of extra help required for adequate performance.
6 = Has chosen not to perform though has demonstrated ability within the past year.
7 = No opportunity to perform within the past year.
8 = Unsure.
9 = N/A.

Please record answers to the probes.

SRP2 Shopping

In the past month have you shopped for yourself?

What sorts of things have you bought?
Do you find any difficulties using the shops?

Rate SRP2 Shopping

NB For calculating the SPI total score 6 and 7 are scored as 2.

Appendix 2: SPQ sample item

SRP2 Shopping

Went into shops and purchased goods	0
Only went into shops when accompanied by a family member, another patient or member of staff	1
Resisted going into shops even if accompanied	2

Acknowledgements, references and author details are given at the end of the accompanying paper (pp. 810–816).

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Day Care in an Inner City

II. Quality of the Services

FRANK HOLLOWAY

Seven units providing psychiatric day care to residents of an inner-city area were surveyed. The extent to which the clinical and special problems of attenders were adequately managed by the services was measured using a 'needs-assessment' technique. Units differed in the proportion of clinical and social problems that were rated as 'unmet needs', although the extent of 'unmet need' was not clearly related to the morbidity of attenders at a unit or the available staffing.

A number of reviews of the extensive empirical literature that now exists in the field of psychiatric day care have recently been published (Herz, 1982; Wilkinson, 1984; Rosie, 1987; Creed *et al*, 1989). One general feature of this literature is a failure to provide an adequate account of the process of day care (Herz, 1982). 'Process' refers to the service provided: whether it meets users' needs and offers appropriate and effective treatment deployed in an efficient and cost-effective manner (Shepherd, 1988). This paper employs a 'needs-assessment' technique developed at the Medical Research Council Social Psychiatry Research Unit (Brewin *et al*, 1987) to investigate the quality of care provided by day services in an inner-city catchment area. The needs-assessment technique produced a measure of the extent to which attenders' clinical and social problems were being adequately managed by the services, and allowed comparisons to be made between units. A companion paper (pp. 805–810) describes the characteristics of the users of day care in an inner-urban catchment area who were in prolonged psychiatric contact.

The aims of the study were to relate the extent to which units met the needs of their 'prolonged-contact' attenders to the resources available at each unit and the morbidity of attenders. It was hypothesised that needs would be more likely to be met at units that were better staffed.

Information on the seven units serving the catchment area was collected systematically using a structured interview which provided data on the staffing, available and occupied places, referral policies, and organisation of each unit. The types of treatment and the activities provided at the unit were also recorded. Respondents (in the case of the day hospital, the senior nurse; in the case of the day centres, the entire staff team) were also asked a number of open-ended questions about the purpose and philosophy of the unit and the difficulties that had been encountered in meeting the needs of attenders. In addition, each unit was asked to provide a copy of its operational policy.

Table 1
Resources of day settings

	Day hospital A	Day hospital B	Day centre A	Day centre B	Day centre C	Work centre	Remploy factory
Total care staff	15	–[1,2]	5	6	6	3	–[1,2]
Places per day	"80"	"80"	"40"	–[1]	"45"	24	–[1]
Clients on books	101	*c.* 130	104	106	82	19	126
Average daily attendances	50	–[3]	25	23	26	18	–[1]
Daily attendances per care staff	3.3	–[3]	5	3.8	4.3	6	–[1]

1. Not applicable to setting.
2. See text.
3. Not known.

Table 1 summarises data on the staffing of the units and the numbers of attenders. Because in day hospital B staffing levels included cover of an attached in-patient facility, and in the Remploy factory staff were not employed to provide care, staffing levels are not reported for these units. The day hospitals had more staff than the other units, and ready access to a whole range of disciplines. The social-services day centres were staffed by qualified and unqualified social workers. The work unit had qualified occupational-therapy and social-work staff. A higher proportion of day-hospital patients on the register actually turned up to the unit each day than did attenders on the books of the social-services day centres. Attendance at the work centre and Remploy factory was very regular.

Except for the Remploy factory, which solely provided sheltered work, all units offered individual counselling. However, most activities in the units involved groups. The two day hospitals had much more varied programmes than the other units, offering a comprehensive range of treatment including group psychotherapy, social-skills training, anxiety management, relaxation training, and groups focused on activities of daily living. Day centre B (a 'community mental health centre') offered only counselling, family therapy and a recreational programme, which was on a drop-in basis. Only 10 out of the 110 prolonged-contact attenders in the sample had access within their unit to work training or paid work, which was unavailable within the catchment-area day hospital and as a matter of policy not provided by the social service department day centres.

Staff at all units except the Remploy factory and day centre C stated that they provided individualised programmes, although observation suggested that such programmes were more theoretical than real in most units, as was the stated development of client–unit contracts. Five units made a distinction between attenders receiving active 'treatment' programmes and those receiving 'support'. This extended to allocating separate days or times of the day for attendance in two units (day hospital A and day centre A). Centre C was, during the study, in considerable organisational disarray. It subsequently closed for a period of refurbishment and reopened with a completely new staff group. Only day hospital B offered a service at evenings or weekends. In two of the units not under the National Health Service (NHS) (day centres A and C) a community psychiatric nurse visited regularly to monitor clients' mental state and give depot antipsychotic injections.

Method

This study used a normative, or expert-defined, definition of need (Bradshaw, 1972). 'Need' was present when a patient experienced a significant clinical, behavioural or social problem in one of the 24 problem areas that were rated. The companion paper (pp. 805–810) presents the methods employed in rating these problems. Need was 'met' when it had attracted an appropriate intervention from the services or informal carers. When a problem was not responded to, or the response was not optimal, an 'unmet need' was present. Unmet need was not rated as present when no intervention was currently possible; for example, in the face of refusal of a therapeutic intervention.

An intervention schedule was developed. When a problem was rated as present it was discussed in detail with a staff respondent. Interventions currently provided for the problem were reviewed, together with interventions that had been provided in the past year or refused. These were compared with a standard list of interventions for each problem. (The list of interventions may be said to represent good psychiatric rehabilitation practice, and consists, with slight modifications, of the interventions produced for the Camberwell Needs for Assessment (Brewin *et al*, 1987). Brewin *et al* have provided evidence for the appropriateness of these interventions.) A raters' manual was produced which provided a detailed description of each intervention, together with advice on making ratings. As an example, the interventions assessed for the common item 'delusions and hallucinations' are shown as Appendix 1. The rating scale employed to assess interventions is shown as Appendix 2.

An example of the use of the schedule is provided by a 22-year-old woman who had been attending a psychiatric day hospital for two years following recovery from an acute schizophrenic episode. When assessed, she was noted to be experiencing marked symptoms of anxiety in crowds and on buses, which were of recent onset, together with some degree of distress over problems with her housing. She was not psychotic, and showed no other clinically significant problems (although she had been mildly depressed in the month). Staff were unaware of her anxiety symptoms. For this problem she was therefore rated as being in 'unmet need' of assessment with a view to initiating behavioural psychotherapy. She had refused attempts to discuss her worries over her housing, which were well known to staff, and otherwise appropriate interventions (problem-focused and emotion-focused counselling) were rated as inappropriate due to refusal.

Interventions were arranged hierarchically in the intervention schedule and lower-ranking interventions were either less generally effective or were of a palliative rather than a potentially curative nature. When a problem was managed by a low-ranking intervention (e.g. all meals provided in a hostel for someone unable to cook), an unmet need was rated, if a higher-ranking intervention had not been given recent or adequate trial (e.g. remedial skills training). The intervention schedule provided ratings of the treatment and care actually offered to the patient for each clinically significant problem, together with ratings of any intervention not currently being offered but felt to be appropriate (indicating an unmet need).

In order to investigate the inter-rater reliability of the schedule, a small reliability study was carried out by undertaking parallel interviews with the same staff member about a number of day-hospital patients. Ratings of the intervention schedule were made by the research interviewer and a second rater, who had read the rating manual and received only very brief training in the principles of the schedule, but was highly experienced in the field of psychiatric rehabilitation. Four cases were rated. They had a total of 28 clinically significant problems, including both clinical and social problems, out of a potential total of 96 problems. The two raters agreed on the needs status of 21 of these problems, disagreeing over 7 problems (75% agreement). This study offers some evidence for the reliability of the needs-assessment judgements made during the study, particularly in view of the lack of training of the second interviewer. It may be compared with an impressive 98% agreement between raters in needs status reported by Brewin *et al* (1987), who used the more complex original version of the needs-assessment procedure.

Results

The 110 day-care users in the sample had a total of 665 clinically significant problems. Of these problems, 212 (32%) were rated as unmet needs. Table 2 shows the problems and unmet needs, and the ratio of one to the other for each problem. Unmet need was particularly commonly rated for the items 'slowness and underactivity', 'side-effects of medication', 'drug/alcohol abuse', 'managing money' and 'use of public transport'.

Table 2
Clinically significant problems and unmet needs of 110 day-care users in prolonged psychiatric contact

	Attenders with problem		Attenders with unmet need	Ratio of unmet needs: problems
	No.	%		
Personal hygiene	13	(12)	3	0.23
Shopping	26	(24)	7	0.27
Cooking	28	(25)	9	0.32
Household chores	25	(23)	5	0.20
Care of dependants	2	(2)	1	0.50
Managing money	23	(21)	12	0.52
Use of public transport	20	(18)	12	0.60
Use of amenities	30	(27)	8	0.27
Leisure activities	16	(14)	6	0.37
Literacy/numeracy	17	(15)	2	0.12
Decision-making	22	(20)	7	0.32
Social skills	33	(30)	12	0.37
Material welfare	20	(18)	3	0.15
Positive psychotic symptoms	29	(26)	14	0.48
Slowness and underactivity	20	(18)	10	0.50
Depressed mood	42	(38)	15	0.38
Other neurotic symptoms	38	(34)	17	0.45
Impaired memory/ concentration	57	(52)	16	0.28
Physical illness	40	(36)	3	0.07
Side-effects	33	(30)	21	0.64
Drug or alcohol problem	16	(14)	8	0.50
Aggression (to self or others)	7	(6)	3	0.38
Socially embarrassing behaviour	25	(23)	7	0.28
Psychosocial distress	83	(75)	8	0.10

The commonest form of intervention suggested was some form of skills training (69 cases) to remedy a deficit in social functioning. This training was not available in a number of the settings; even where it was available, places in skills-training groups were limited because of lack of resources.

Alteration in, or review of, psychotropic or physical medication was recommended in 43 cases. Review of anti-psychotic medication was suggested in 20 patients who were showing side-effects. Prescription of, or increase in, antidepressant medication was felt to be required for 11 patients with evidence of depression. (Results of a review of psychotropic prescribing to the sample have been reported (Holloway, 1988*b*).)

For 38 cases, the unmet needs identified required the development of a structured programme to monitor and modify an attender's deviant behaviour or to provide a carefully graded set of activities to improve concentration or help a disorganised patient through the day. Day units did not, in general, cope well with the task of developing a response to deviant behaviour, such as aggression or drug/alcohol abuse. The most likely response to such behaviour when it was recognised was discharge from the unit.

Table 3
Problems, met needs and unmet needs of 110 prolonged-contact attenders by unit

	Day hospital A ($n=64$)	Day hospital B ($n=4$)	Day centre A ($n=17$)	Day centre B ($n=13$)	Day centre C ($n=6$)	Work centre ($n=3$)	Remploy factory ($n=3$)
Unmet needs	124	7	38	21	18	1	3
Met needs	287	20	85	32	12	14	3
Total problems	411	27	123	53	30	15	6
Unmet needs as % total problems[1]	30	26	31	40	70	7	50

1. Significant differences between units in number of problems rated as unmet needs: $\chi^2=20.45$, 6 d.f., $P<0.01$.

All but two of the day units in the study (day hospital B and the work centre) had great difficulty in providing a highly structured environment tailored to an attender's behavioural problems.

Counselling or the provision of specific coping advice to the patient was felt to be required in 23 cases. Some attenders needed someone to talk to about distressing symptoms and to provide support and reassurance where symptoms were intractable. Symptoms might also merit specific advice to the patient or relatives on developing coping strategies. Patients experiencing positive psychotic symptoms tended to be receiving adequate, or even excessive, medication, but to be in need of these interpersonal types of treatment. Staff working outside health-service settings had no specific training in psychiatry, and were offering an essentially lay perspective to their clients when discussing symptoms and how to deal with them. However, staff in both NHS and non-NHS units were reluctant to discuss symptoms with their patients/clients, and no one reported having received training in the provision of coping advice.

Behavioural assessment and/or treatment was felt to be necessary for 18 patients, in the main to treat neurotic symptoms such as phobic anxiety or obsessional symptoms. This was only available at the two day hospitals. Skilled psychological assessment was occasionally felt to be indicated for other problems, for example for a man who complained of violent outbursts of temper. A small number of very intractable problems that were not being addressed were felt to require some form of sheltered or prosthetic environment. The remaining interventions were very heterogeneous, including, for example, adult education for someone with a literacy problem.

Comparisons between units

Table 3 shows the number of 'unmet' and 'met' needs noted at each unit. On average, one out of every three problems was rated as an unmet need, although 36 attenders had no unmet needs. The proportion of problems rated an unmet need varied between 7% at the work centre and 70% at day centre C. Day hospital A and day centre A had almost identical ratios of unmet needs to problems (30% and 31%), while at day centre B the ratio was somewhat higher (40%). Overall, there were significant differences in the numbers of needs that were met and unmet in the units ($\chi^2=20.24$, 6 d.f., $P<0.01$). Inspection of the χ^2 table reveals that these differences are mainly due to two outliers, centre C and the work centre, and to a lesser extent centre B, the 'community mental health centre'.

Unmet need was significantly less common among day-hospital attenders for only two problem items: 'drug/alcohol abuse' and 'cooking'. Unmet need was noted in only one of the nine day-hospital attenders with a drug or alcohol problem, but in all seven day-centre attenders with such a problem. Six of these users were at day centre B. Only two of the 14 day-hospital attenders who had been rated as having a significant problem with cooking skills were felt to have an unmet need, compared with seven out of 14 attenders in non-hospital units with this problem. Attenders at day centre C were particularly unlikely to have their self-care problems addressed: eight out of the nine self-care problems noted among the six cases were rated as an unmet need, compared with one out of four such problems for the sample as a whole.

Table 4 brings together data on the resources of the units (represented by the mean number of attenders per staff member), the morbidity of attenders (represented by the mean total number of clinical, behavioural and social problems rated at each unit) and the efficacy of the units (represented by the percentage of problems rated as unmet needs at each unit). There was no evidence that the significant differences between units in the proportions of

Table 4
Resources, problems and unmet needs in day units serving 110 prolonged-contact attenders

Unit	Number of attenders in sample	Attendances per staff member	Mean number problems per attender	Percentage unmet need
Day hospital A	66	3.3	6.4	30
Day hospital B	4	–[1]	6.7	26
Day centre A	17	5.0	7.2	31
Day centre B	13	4.0	4.1	40
Day centre C	6	4.3	5.2	70
Work centre	3	6.0	5.0	7
Remploy	3	–[2]	3.0	50

1. Not known.
2. Not applicable to unit.

problems that were identified as unmet needs could be explained by differences in morbidity among attenders or by differences in the resources available to provide treatment and care. The similarities between the morbidity of attenders and the proportions of problems that were unmet needs at day hospital A and day centre A contrast starkly with the higher level of staffing available at day hospital A.

Discussion

The results of this study, which focused on the needs of a sample of day-care attenders from a defined catchment area in prolonged contact with a particular set of psychiatric services, cannot be generalised. The study provided no data on the use of 'acute' day care within the district (which was, in fact, minimal). Its results are in apparent contradiction with the findings of the Camberwell High Contact Survey (CHCS), which used similar methods on the adjacent South Southwark psychiatric service (Brewin *et al*, 1987, 1988; Brugha *et al*, 1988). The CHCS found that whereas morbidity was similar among day-hospital and day-centre attenders, unmet need was much commoner among day-centre clients (Brugha *et al*, 1988). However, the CHCS identified a day hospital serving a small number of attenders in their sample which was very similar to the day centres in terms of the proportion of problems that were rated as unmet needs. This was in fact day hospital A.

Since this was a cross-sectional study, it is possible that, at admission, attenders of NHS units were more disabled than attenders at the other units (or vice versa). It is therefore possible, for example, that day hospital A may have been more successful in the early stages of 'treatment' or 'rehabilitation' than day centre A. A comparative prospective study would be required to address this issue. However, the results suggest that the resources available in day hospital A were not being used appropriately for the prolonged-contact attenders who were assessed. The key problem may have been a failure to develop systematic plans of management and to review these plans regularly. Regular review by all responsible professionals involved in a patient's care has been advocated as the single most important step in ensuring that the needs of people receiving community care are met (Wykes *et al*, 1985). The multi-faceted nature of need among the chronically mentally ill and the slow rate of change that may be expected from treatment requires the development of structured techniques for assessment and for the recording of data.

An analysis of the unmet needs that were identified suggests that the medical management of the users was not optimal, and that a thoroughgoing review of local drug-treatment practices relating to the chronically mentally ill was required (Holloway, 1988*b*). Lack of resources accounted for the limited amount of skills training that was being provided. None of the main day units within the district service was capable of providing a highly structured environment suitable for patients severely handicapped by negative symptoms, or within which programmes of behaviour modification could be carried out.

This study has applied the novel technique of needs assessment (Brewin *et al*, 1987). Needs assessment is based on the proposition that the aim of psychiatric services is to reduce or contain morbidity, itself a sophisticated concept (Wing, 1972). Brewin *et al* (1987) argue that need is not present when there is no possible effective intervention (e.g. when a patient refuses antipsychotic medication, although suffering from delusions or hallucinations). This viewpoint stems directly from a desire to link a treatment plan with the assessment of need (Shepherd, 1988). In clinical practice such refusal is common, and may lead to a prolonged and on occasion painful negotiation between caring agencies and the reluctant client. Part of the skill of working with the chronically mentally ill is to engage people with the services, often by addressing first those issues perceived by the client to be relevant, such as welfare benefit and housing needs.

Although evidence for the reliability of the modified needs-assessment procedure adopted in this study is sketchy, the procedure proved to have considerable face validity, at least for staff used to working within a problem-orientated framework. One inevitable limitation in the study design was that it provided no evidence that patients would, in fact, benefit if their 'unmet needs', as defined, were met by the provision of treatment or care. There is remarkably little evidence for the efficacy of practices adopted in the field of psychiatric rehabilitation, particularly in naturalistic settings with unselected populations of patients. Testing and refining the efficacy of the interventions proposed in the needs-assessment schedule represents a major research challenge for the future.

Using the needs-assessment technique, two centres stood out. One, the work centre, appeared to be very successful in meeting the needs of its clients who came from the catchment area, while another, day centre C, was very unsuccessful. The impending closure of day centre C, lowering staff morale and promoting uncertainty over the future among both staff and users, may have explained its poor performance. The success of the work centre may be related to the close links that its staff maintained with referring agencies, who would be expected to attend to specific psychiatric or social-work issues. In contrast with day hospital A, which lacked clear goals or a coherent operational policy, staff at the work centre had clear goals for the unit and a limited remit.

Although the seven settings included in the study differed considerably in organisation, aims and resources, these differences were perhaps less striking than the similarities between the units. These similarities may reflect the nature of the task facing those offering day care to the long-term mentally ill. Day-hospital and day-centre attenders presented very similar kinds of problems to the services, both in terms of symptoms and abnormal behaviour and in terms of impairments in social functioning. It follows logically from these results that the distinction between day hospital and day centre should be abandoned. Skills may be available within the NHS facilities which could be meeting equal if not greater need among attenders at non-NHS units.

It is apparent from discussion with staff at the units that co-ordination between elements of the day-care service in the area was poor, at both a planning and an operational level. In most units, staff felt isolated from the rest of the local services and from their own management. Social-services staff often had difficulty in obtaining help for their clients from the hospital, while hospital-based staff had little perception of what went on outside their own unit. The results of the study suggest a need within the catchment area to undertake a multi-agency review of the provision of day care and community support for the chronically mentally ill, and to develop specific skills in psychiatric rehabilitation.

The needs-assessment technique proved a powerful, if labour-intensive, tool in identifying deficiencies in the service system. However, other techniques might prove more practical for the average service. These might include the characterisation of attenders on basic socio-demographic and diagnostic parameters, structured interviews with care staff and attenders about the functioning of units, and comparisons between the existing service system and alternative models for the provision of day care and community support (Holloway, 1988*a*).

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Appendix 1: Interventions for positive psychotic symptoms

1. Medication
2. Supervision and monitoring of medication
3. Domiciliary visiting to ensure compliance
4. Support and reassurance to the patient
5. Coping advice to the patient
6. Coping advice to a relative
7. Expressed emotion or family intervention
8. Sheltered environment (part of the time)
9. Sheltered environment (full time)
10. Other (to be specified)

Appendix 2: Intervention rating scale

0 = Intervention not necessary (problem below threshold, other appropriate interventions available)
1 = Intervention provided and effective or potentially effective (potential means less than three months' trial)
2 = Intervention provided not fully effective but remains appropriate
3 = Overprovision (includes interventions provided for more than three months without evidence of efficacy)
4 = Intervention not appropriate now, due to failure after a trial in the past year, refusal, or on clinical grounds
5 = *UNMET NEED*: intervention not given but appropriate (includes inadequate current trial or lack of an adequate trial in the past year)
8 = Unsure
9 = Missing data

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The Nature and Severity of Disabilities in Long-Stay Psychiatric In-patients in South Glamorgan

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Long-stay psychiatric in-patients in South Glamorgan were reviewed using the MRC Needs for Care assessment. The majority were middle aged or elderly and were severely disabled, with problems encompassing symptoms/behavioural difficulties, social skills, and physical health. In most, long-standing psychiatric illness was compounded by physical illness and cognitive deficits as age advanced, producing care needs that were greater than existing community services could meet.

In the UK, as in some other Western countries, the chronic mentally disabled have been the focus of public concern for at least four decades (Kendell, 1989). There have been reports of scandals, which in the 1970s were mainly associated with psychiatric hospitals but, more recently, with care in the community (Thornicroft & Bebbington, 1989). It seems likely that the running down and closure of psychiatric hospitals, a policy which in many cases has much to commend it, has compounded the inadequacy of community provision and contributed to the poor quality of life of some of the mentally disabled living in the community. Health ministers are now insisting that hospital closures are not a primary aim of health policy for the long-term mentally ill (National Unit for Psychiatric Research and Development, 1988).

Among the chronic mentally disabled, the residual long-stay hospital population is still important. It contains many of the most severely disabled and disturbed, and the cost of their service requirements is substantial. However, there is a dearth "of evidence both about the clinical characteristics of patients requiring long term or oft recurring hospital care and about the comparative costs of treating severely disabled patients in hospital and in the community" (Kendell, 1989). Nevertheless, long-stay bed numbers continue to be reduced, a number of psychiatric hospitals have been closed, and there are plans to close others.

In South Glamorgan, Whitchurch Hospital, the main psychiatric unit, has not as yet been given a closure date. Built in 1909 in the village of Whitchurch three miles from the centre of Cardiff, it is now suburban. Both the hospital and an annexe for long-stay patients (in another suburb) are on large and potentially valuable sites. In the South Glamorgan Health Authority 10-year plan the annexe is due for early closure, and plans are being considered for the commercial development of the Whitchurch site and part of the hospital building itself. It is expected that the hospital long-stay population will contract further, and a few small community developments are already at the planning stage. However, there is no overall development plan for services for patients with high dependency needs.

The primary aim of the inquiry we undertook was to determine the problems and needs of the long-stay in-patient population (continuous stay of a year or more) for the county of South Glamorgan and the Rhymney Valley in Mid-Glamorgan (total population 420 000), its total number and the numbers in various subgroups, as well as the extent to which needs were being met by existing services. It might then be possible to suggest improvements in current service provision, and more generally, to provide a sound empirical basis for the planning and organisation of future services. We report here on the nature and severity of disabilities in the total population.

Method

Whitchurch Hospital provides 400 beds in seven long-stay wards, and an annexe seven miles away has 40 beds. A few patients become long stay on acute admission wards in the main hospital and in two general hospitals in the district.

Regular formal interdisciplinary assessments of patients' problems and needs have been held on long-stay wards and the annexe for over 20 years (generally twice-yearly for each patient). Since 1977 the assessment meetings have been organised by the hospital's computerised Information Coordinating Centre (ICC), which has provided the documentation, including details of previous behavioural ratings on the standardised 'REHAB' scale (Pryce & Hall, 1980).

Some indication of the size of the long-stay in-patient population compared with the numbers of mentally disabled

Table 1
Number of psychiatric patients in contact with the continuing care services of the South Glamorgan Health Authority

	Men	Women	Total
Long-stay in-patients[1]	77	97	174
Long-attending day patients[2]	80	49	129
Depot clinic attenders[3]	77	47	124
Receiving depot medication from community nurses[3]	45	67	112
Total	279	260	539

1. Current admission >1 year, 25 March 1988.
2. Current attendance >1 year, March 1988.
3. April 1988.

people in contact with other services at the time of the survey, is given in Table 1. Doubtless there were some not in contact with any service.

Figure 1 shows the rate of increase in the number who had stayed in hospital a year or more since 1978, and of the decrease in the number who had become long stay before 1978. At the time of the survey, around 60% had become long stay over the previous 10 years. During each of these 10 years, approximately two-thirds of those who had become long stay were middle aged or elderly.

All patients who had been resident for a year or more in South Glamorgan psychiatric hospitals or units on 25 March 1988, excluding those in psychogeriatric wards or with a primary diagnosis of dementia, were initially selected from ICC data. Of these 180, the research team found a further six with dementia, and during the year of the inquiry six died and 12 were discharged before they could be assessed, leaving a total sample of 156.

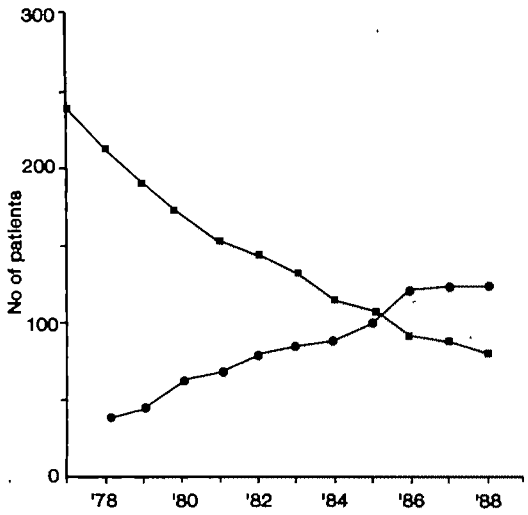

Fig. 1. Number of persons in psychiatric units in South Glamorgan who stayed a year or longer (a) admitted in 1977 or earlier (■), (b) admitted 1978–88 (●) (end-of-year-figures).

The data collected were as follows:

(a) Demographic data – sex, age, marital status on admission
(b) Psychiatric illness – clinical diagnosis, time since first contact with in-patient services, length of current admission
(c) Research team assessments – the NFC, SBS, MMSE and AIMS (see below).

The researchers consisted of three psychologists, three psychiatrists and a senior nurse, all with experience of working with chronic patients. The main instrument used was the Needs for Care assessment (NFC; Brewin *et al*, 1987) which specifies rules for defining problems in 20 areas of clinical and social functioning, and sets down decision rules for classifying problems with reference to a 'met need', 'unmet need', or 'no need'. The schedule was completed by interviewing the patient's primary nurse, ward sister or charge nurse, who also provided information for the Social Behaviour Schedule (SBS; Wykes & Sturt, 1986). The researcher carried out a standard assessment of each patient's cognitive level using the Mini-Mental State Examination (MMSE; Folstein *et al*, 1985), and when necessary assessed the level of dyskinesia with the Assessment of Involuntary Movements Scale (AIMS; National Institute of Mental Health, 1974). Case notes and other staff were consulted as necessary.

The use of the Needs for Care assessment on a long-stay in-patient population

The NFC was developed primarily for high-dependency day patients. There were several reasons for its use in this study. It is designed for people with similar clinical and behavioural characteristics, and gives detailed definitions of problem areas. It also defines commonly accepted interventions for problems, and gives rules for defining a patient's needs status in relation to problems and actual interventions.

The team carried out an initial pilot study to familiarise itself with the definitions and rules and had the benefit of a day's seminar with one of the authors of the schedule. In the main study, the final ratings were made by the researcher without further consultation. In a later reliability study, 21 pairs of researchers rated taped interviews with between five and 14 subjects. In the four items chosen for analysis, the agreement was as follows: positive psychotic symptoms, 72%; socially embarrassing behaviour, 81%; personal hygiene, 86%; use of public amenities, 59%.

In most cases, the data required for the NFC were readily available from the primary nurse, and the assessment was fairly easy to complete. However, problems were experienced with Part B of the schedule (skills and abilities) when rating patients who were old and/or severely handicapped. Such patients were often unlikely ever to achieve or require some of these skills, for example for work or use of public transport. In such cases, the NFC Manual suggests either rating certain Part B items as 'not applicable' for the whole sample, or rating skill status as 'unknown' and needs status as 'met need'. We rejected both suggestions, the first since variable but often sizeable minorities of our sample were

Table 2
Symptom and behaviour problems[1] in long-stay psychiatric in-patients in South Glamorgan

	Current problem[2]	Problem in recent past[3]	No problem	Insufficient information
Socially embarrassing behaviour	70 (44.9%)	9 (5.8%)	76 (48.7%)	1 (0.6%)
Physical symptoms and disease	61 (39.1%)	16 (10.3%)	77 (49.4%)	2 (1.3%)
Slowness and underactivity	57 (36.5%)	4 (2.6%)	95 (60.9%)	0 (0%)
Positive psychotic symptoms	51 (32.7%)	21 (13.5%)	78 (50.0%)	6 (3.8%)
Dangerous and destructive behaviour	44 (28.2%)	11 (7.1%)	101 (64.7%)	0 (0%)
Neurotic symptoms	34 (21.8%)	5 (3.2%)	116 (74.4%)	1 (0.6%)
Distress linked with long-term social problems	19 (12.2%)	2 (1.3%)	135 (86.5%)	0 (0%)
Tardive dyskinesia	17 (10.9%)	1 (0.6%)	136 (87.2%)	2 (1.3%)
Dementia and organic psychosis	16 (10.3%)	0 (0%)	136 (87.2%)	4 (2.6%)

1. Section A of NFC.
2. Over last month.
3. Over last 2 years (but not currently).

likely to use or need most of the skills, and the second because the conditions specified were not satisfied since the skill status was often known. Instead we rated individual cases as 'not applicable', which is equivalent in this study to 'skill or ability seems unlikely ever to be required because of age and/or severity of handicap'. A formal assessment was not required and might indeed generate unnecessary needs by NFC rules.

Results

There were 65 men and 91 women. The men were somewhat younger (mean age 57.5 years (range 27–87) v. 64.1 years (29–88); whereas 60% of the men were under 60, 60% of the women were over 60. Only 30.4% of the men had ever been married compared with 45.7% of the women. (Comparable figures for the general population of Cardiff were 55.4% (men) and 61.5% (women) (Welsh Office, 1986).)

Two-thirds of the sample (109) were in the four general long-stay wards and the annexe, 25 in a unit for the chronically disturbed, 12 in a resettlement ward, seven in acute admission wards, and three in a locked disturbed/forensic ward.

In 64% of the sample the primary diagnosis was schizophrenia, and in 18% it was depression, while the rest were given various diagnoses including personality disorder (7%) and brain damage from various causes. Severe cognitive impairment was common, with 48.5% scoring below 20 on the MMSE (Dick *et al*, 1984). Two-thirds of the low scorers were aged over 68. Physical illnesses and disabilities were common, and caused recent or recurrent problems in half the sample (Table 2). The mean length of illness was 26.4 years; 44% had been ill for between 20 and 39 years and 20% for 40 years or more; there were no sex differences.

The main clinically significant problems in the last month were socially embarrassing behaviour, physical symptoms, slowness and underactivity, positive psychotic symptoms, dangerous and/or destructive behaviour, and neurotic symptoms. In addition, smaller numbers had problems stemming from socially determined distress, tardive dyskinesia, or organic psychosis. Problems occurring only during the previous two years (but not the last month) were mainly related to psychotic symptoms, physical symptoms and dangerous and/or destructive behaviour.

Problems related to skills and abilities

Thresholds for competence and performance in the NFC are low. Nevertheless, in eight of the 11 areas only a third or less were judged to be competent. In addition, just over half were judged to have no difficulty with conversation and social mixing, and two-thirds to be able to read, write or do simple arithmetic (Table 3).

For a substantial number of subjects, in all areas except personal hygiene and communication, the raters judged that the skills assessments were 'not applicable' because age and/or severity of handicap/illness made it unlikely that the skills could be acquired or would be needed. In particular, this applied to employment and managing one's own affairs, but also to household shopping, getting meals, and use of money, and to a lesser extent to household chores, use of public transport or amenities, and basic education. A statistical comparison of the 47 subjects with 7–10 'not applicable' (NA) ratings, with the 49 with none or one, showed that the former were more likely to be older ($P=0.0001$), to be slow and underactive ($P=0.0009$), to have physical problems ($P=0.01$), to have an organic psychosis ($P=0.02$), to have severe cognitive deficits ($P<0.02$) and to show socially embarrassing behaviour ($P=0.02$). This comparison corroborates the criteria used for NA ratings.

In a minority of cases, there was uncertainty in some areas as to subjects' competence. This applied to shopping, getting meals, and use of public transport, where in a quarter of the sample, available information was insufficient to make a judgement, as it was to some extent for use of public amenities and basic educational skills. This uncertainty indicates an unmet need for assessment by staff, and will be considered more fully in a subsequent paper.

Table 3
Skills and abilities of long-stay psychiatric patients in South Glamorgan[1]

	Current[2] problem	Recent[3] problem	No problem	Insufficient information	Not applicable
Personal hygiene	86 (55.1%)	14 (9.0%)	55 (35.3%)	0 (0%)	1 (0.6%)
Household shopping	19 (12.2%)	2 (1.3%)	20 (12.8%)	40 (25.6%)	75 (48.1%)
Getting meals[4]	19 (12.2%)	2 (1.3%)	20 (12.8%)	40 (25.6%)	74 (47.4%)
Household chores	30 (19.2%)	5 (3.2%)	60 (38.5%)	7 (4.5%)	54 (34.6%)
Public transport	27 (17.3%)	0 (0%)	38 (24.4%)	37 (23.7%)	54 (34.6%)
Public amenities[4]	45 (28.8%)	1 (0.6%)	52 (33.3%)	23 (14.7%)	34 (21.8%)
Education[4]	7 (4.5%)	0 (0%)	104 (66.7%)	15 (9.6%)	29 (18.6%)
Occupation	14 (9%)	1 (0.6%)	14 (9.0%)	10 (6.4%)	117 (75.0%)
Communication	65 (41.7%)	1 (0.6%)	86 (55.1%)	1 (0.6%)	3 (1.9%)
Use of money	26 (16.7%)	1 (0.6%)	29 (18.6%)	30 (19.2%)	70 (44.9%)
Manage own affairs	5 (3.2%)	0 (0%)	10 (6.4%)	24 (15.4%)	117 (75.0%)

1. Section B of NFC.
2. No evidence of skill at any time over past year.
3. Within past 2 years (but not currently).
4. One case is listed as missing for each of these areas so that the row total = 155.

The data were analysed to give the mean number of clinically significant problems per patient, both for the 9 symptoms or types of behaviour, and the 11 skills and abilities. For the former, the means for current and recent problems were, respectively, 2.4 and 0.4; for the latter, 2.2. and 0.2. In addition, of the 11 social skill items, an average of 4.0 were rated NA and 1.5 as 'not known'. Bearing in mind our criteria for NA ratings, the total mean number of current problems for skills and abilities was probably around 6. A number of the 'not known' ratings also, if known, would probably be rated as problems.

Current problems in the present sample compared with those in a sample of high-dependency day patients

Brugha *et al* (1988) have published NFC data on a group of 145 high-dependency day patients aged 16–65. Compared with the present sample, this was a younger group, with 30% aged under 30 (7% in the present sample), a shorter length of illness (by 10 years), and a higher proportion of men (55%); the percentages with a diagnosis of schizophrenia and with physical problems were similar.

The numbers with current symptom and behaviour problems were markedly greater in the in-patient sample as regards dangerous/destructive behaviour (28%/6%), slowness and underactivity (37%/18%), socially embarrassing behaviour (45%/29%), and dementia and organic psychosis (10%/3%). They were similar for positive psychotic symptoms (33%/36%) and neurotic symptoms (22%/23%); and less for distress linked with long-term social problems (12%/23%). The data for skills and abilities are more difficult to compare because of the high number of NA ratings in nine of the 11 items in the present sample. For the other two items, the comparisons indicate higher numbers with deficits in the in-patient group – 55% compared with 21% for personal hygiene, 42% v. 31% for communication skills. As already indicated, NA ratings in the present study were given to subjects who were severely disabled. If these were added to those with 'current problems', two to six times as many in-patients as day patients would have problems with household shopping, getting meals, household chores, use of public transport or public amenities, use of money, and managing their own affairs.

Discussion

The hospital and annexe provided good physical ward amenities with easy access to work and occupational departments, and to psychiatric nurses and other professional staff. Regular formal multidisciplinary reviews of patients were carried out with the aim of identifying and dealing with the problems presented by chronic illness and social disability. Every patient, except one, in the present sample had a detailed care plan, and was receiving a range of medical, social and psychological treatments. Nevertheless, patients as a whole remained severely disabled. Reasonable levels of care were achieved, a few patients improved and one or two were discharged each month; but for the majority their level of self-sufficiency and quality of life remained well below normal standards.

The service responded to the needs of individuals both by planned interventions based on twice-yearly formal assessments, and on an *ad hoc* basis as new needs arose demanding attention. The extent to which needs were met could be gauged from NFC ratings. As will be reported in detail elsewhere, there were few unmet needs for interventions to deal with symptoms/behavioural difficulties, although in a sizeable minority there was an unmet need for the assessment of skills and abilities.

The NFC was primarily developed for use with high-dependency day-patients in Camberwell, and data are available for this group (Brugha *et al*, 1988).

As has been shown, our sample was appreciably more disabled and disturbed. REHAB and other data similarly show much greater disability compared with South Glamorgan high-dependency day patients investigated in earlier studies (Pryce, 1972; Pryce *et al*, 1983; Pryce & Preston, 1988). This greater disability accounts for the relatively high number of NA ratings for social skills in our sample. The subjects' disabilities were so severe and numerous that a high level of care would probably always be needed.

The age structure, length of illness, physical problems, and cognitive deficits of the sample suggest that initial disabilities due to chronic psychiatric disorders had been compounded by those due to physical disorders and cognitive deficits as age advanced. At some point, it is likely that increasing disability caused serious difficulties for the disabled person's carers in the community. Relatives, who can provide high level care well into a disabled person's middle age (Pryce *et al*, 1983; Pryce & Preston, 1988), and are the main carers in the district, may themselves have become incapable of care due to age and illness.

However, the barriers to long-stay hospital care were high. Bed turnover on long-stay wards was slow, and with the reduction in bed numbers, vacancies were few and infrequent. The initial admission of severely disabled people was therefore nearly always to acute admission wards, where they often had to stay a long time before transfer. In our sample there were seven such patients still awaiting transfer after over a year. Long-stay patients on acute wards reduced the number of available beds, which led to difficulties when the demand for acute admission was high. It was, therefore, tempting to discharge such patients prematurely to settings offering less than adequate care. In effect, transfer to a long-stay ward was likely to occur only after the failure, and sometimes the repeated failure, of care in the community.

The number of long-stay in-patients, in a district providing a reasonably good service for the long-term mentally ill, will depend on the numbers in other, non-hospital residential/day-care systems, and on the levels of care that these other systems provide. There should be very few disabled people who are homeless or in prison. In our sample of in-patients, although the general level of disability was high, there were of course variations in patterns and levels of disability. In general, the service met two broad levels of need: for the less disabled, it made up for shortfalls in the provision of types of community services already available, for example at staffed homes, and at homes for the elderly; it also provided for patients too disabled or disturbed for care elsewhere. There is no doubt that the service overall could be improved, and made more acceptable to patients and relatives.

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The Prediction of Chronic Persistent Versus Intermittent Tardive Dyskinesia
A Retrospective Follow-Up Study

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Relatively little is known about the course of TD in patients continuing to receive neuroleptic medication. In a retrospective follow-up study of 192 patients seen two or more times (average 7.7 visits) over 3–55 months in the Yale Tardive Dyskinesia Clinic, 112 (58%) demonstrated a 'chronic persistent' pattern, the remainder an 'intermittent' pattern. The most important predictors of chronic persistent TD, using multiple logistic-regression analyses, included increased age and the presence of non-orofacial TD at baseline.

Since the first report of tardive dyskinesia (TD) (Schonecker, 1957), investigators have learned relatively little about the course of involuntary movements in psychiatric patients who continue to receive neuroleptic medication. This question is clinically important because most such patients ultimately require continued treatment. In addition, the answer to this question may contribute to understanding the aetiology of the disorder. In general, the findings of population-based studies of general psychiatric patients with TD (Uhrbrand & Faurbye, 1960; Crane, 1967; Crane *et al*, 1971; Turek *et al*, 1972; Chien & Cole, 1973; Branchey *et al*, 1981; Seeman, 1981; Smith *et al*, 1981; Wegner & Kane, 1982; Yassa *et al*, 1984; Casey, 1985; Casey & Gardos, 1986; Casey *et al*, 1986; Yagi & Itoh, 1987; Gardos *et al*, 1988) suggest that TD is not always persistent and that it does not progressively worsen over time. However, most of these studies have not included enough subjects or follow-up to allow for an adequate analysis of the demographic and clinical predictors of TD persistence (Gardos & Cole, 1983). If follow-up consists of a single visit, one could mistakenly conclude that patients were improved or worsened when more extensive longitudinal observations would indicate otherwise.

In the Tardive Dyskinesia Clinic at the Connecticut Mental Health Center, we followed 192 TD patients for a mean of 7.7 visits, and this paper reports a retrospective follow-up study of the course of TD in that population.

Method

In 1978 we organised the Tardive Dyskinesia Clinic for research, service and teaching purposes (Glazer & Moore, 1981; Glazer, 1986). Located in the Outpatient Division of the Connecticut Mental Health Center (CMHC), the clinic staff comprises a nurse co-ordinator, faculty psychiatrists, and psychiatry residents who rotate through on a yearly basis. Patients with involuntary movements were identified by clinical staff and referred for evaluation to the clinic. There is good reason to assume that clinical staff referred the majority of cases from the source population of 600–800 out-patient neuroleptic users because, in a prevalence study of patients attending one of the major treatment units in the Out-patient Division (about one half of the population at risk), 78% of the cases of TD identified had already been diagnosed in the clinic (Morgenstern *et al*, 1987*a*).

Included in this report are all 192 of the 228 patients diagnosed between the clinic's inception in late 1978, and 31 December 1981 who were subsequently seen more than once. Using medical records of the regularly scheduled quarterly visits at the clinic, patients were followed retrospectively from the time of TD diagnosis to 30 June 1985. Typically, each patient was seen at the clinic at least once every three months; however, the frequency of visits and duration of participation varies widely among patients. All patients were prescribed neuroleptic medication by treating psychiatrists on an ongoing basis during follow-up. Patients whose neuroleptic medication was discontinued are the subject of separate reports (Glazer *et al*, 1984, 1990) and are not considered here.

Movement severity was measured with the Abnormal Involuntary Movement Scale (AIMS; Guy, 1976) (Glazer, 1988), which comprises ten items (each coded 1–4), seven assessing abnormal movements in different anatomical areas, and three global items assessing general severity, incapacitation, and patient awareness of the condition. The AIMS score used in this study was the sum of the seven anatomical scores only. Inter-rater agreement among the faculty and resident psychiatrists who participated in this study was acceptable (Lane *et al*, 1985).

Psychiatric diagnosis was established with the Schedule for Affective Disorder and Schizophrenia (SADS–L; Spitzer & Endicott, 1978) and Research Diagnostic Criteria (RDC; Spitzer *et al*, 1978). SADS–L interviews were performed by one psychiatric research nurse who had had seven years' experience with schizophrenic patients. Since SADS–L interviews were not performed during the early phase of follow-up, not all patients received research diagnoses.

In addition, the following baseline variables were obtained and, for purposes of analysis, were categorised as follows:

(a) demographic data: age (continuous), socioeconomic status (social class I–III, IV, V (low); Hollingshead, 1975), race (white/non-white), lives alone (yes/no), sex

(b) psychiatric and treatment history: ever (before baseline interview) on depot neuroleptics (yes/no), ever (before baseline interview) on high-potency neuroleptics including fluphenazine, haloperidol, perphenazine, thiothixene and trifluoperazine (yes/no), duration of antipsychotic medication at baseline (0–95 months, 96–155 months, 156 months or more), duration of mental illness at baseline (0–11 years, 12–20 years, 21 years or more), number of psychiatric admissions at baseline (0–2, 3–5, 6 or more), and psychiatric diagnosis (schizophrenic, schizoaffective, other)

(c) TD history: total AIMS at baseline (continuous), non-orofacial TD at baseline (yes/no, defined as a total score of 2 or more on the three non-orofacial components of the AIMS score), duration of TD at baseline (0–14 months, 15–30 months, 31 months or more), and denture use (yes/no).

At each quarterly follow-up visit, a faculty or resident psychiatrist examined the patient using the AIMS and recorded medication status after questioning the patient and reviewing the clinical record. Neuroleptic dose was converted to chlorpromazine equivalent (CPZE) values (Hollister, 1977). Longitudinally defined variables included the number of examinations (2–3, 4–8, 9 or more visits), the difference between the maximum and minimum CPZE drug dose throughout the course of follow-up (less than 20 mg, 21–178 mg, 179 mg or more), the average CPZE during follow-up (continuous), the percentage of visits with changes in anti-Parkinsonian agents (0 not on anti-Parkinsonian medications or no change in dose during follow-up), 1–33%, 33% or more), and change in neuroleptic medication during follow-up (yes/no).

To describe the natural history of TD, we used Schooler & Kane's (1982) typology and applied it to the longitudinal data set. The Schooler–Kane classification system establishes three prerequisites for the diagnosis of TD: (a) at least three months of cumulative neuroleptic exposure; (b) minimum AIMS scores of either 3 for one anatomical area or two scores of 2; and (c) the absence of differential diagnosis. On the basis of these criteria and observed changes in AIMS scores and neuroleptic dosage, we were able to classify each patient at each visit as 'persistent TD' if the three criteria were met on two consecutive examinations.

Schooler & Kane's term 'persistent TD' refers to movements observed on two consecutive occasions. It does not describe the long-term course of TD in a particular patient. In order to describe the overall course of TD, we defined the outcome measure 'chronic persistence' as persistent TD (Schooler–Kane criteria) on at least 50% of all follow-up visits. The remaining patients were classified as 'intermittent TD' cases.

Statistical analysis

To identify which clinical and demographic variables were associated with chronic persistence, crude (unadjusted) odds ratios were computed for each of the above-mentioned categorical variables, using logistic regression (Kleinbaum *et al*, 1982). A modified stepwise procedure was then used to control for confounding among the covariates and to generate a model that best predicted chronic persistence. First, two variables are treated as 'methodological covariates' – total baseline AIMS score and number of visits during follow-up. These methodological covariates were forced into the model because they were regarded (*a priori*) to be confounders of certain other predictors. Next we used a stepwise procedure to select additional predictors for the model. Finally, we added each of the other variables, one at a time, to this 'best' model to see if they altered the results (i.e. adjusted odds ratios) for the other predictors.

Results

For the 192 patients, the mean number of examinations was 7.7 (s.d. 6.4, range 2–33), and the average follow-up was 18.5 months (s.d. 12.3, range 3–55 months). At baseline, the mean age of the group was 46 years (s.d. 14.3); 61% were female, and 78% were white.

We were unable to obtain RDC diagnoses on 41 of the 192 patients because we did not perform research diagnostic examinations when the TD clinic began. Of the 151 patients with RDC diagnoses, 83 (55%) were schizophrenic, 40 (26%) were schizoaffective, and 28 (19%) were other (mostly affective) psychiatric disorders.

The average duration of mental illness for the group was 17 years (s.d. 10.3) and the average number of psychiatric admissions was 4.2 (s.d. 3.5). The average duration of exposure to neuroleptic medication was 10 years (s.d. 6.2) and the average dose of neuroleptic medication was 322 mg CPZE (s.d. 265). The mean baseline total AIMS score was 6.5 (s.d. 3.0) and the estimated average duration of TD at the time of the first examination was 27 weeks (s.d. 21). Of the 104 patients (54%) receiving a total score of 2 or more on the three non-orofacial areas of the AIMS, only one received that score from two non-orofacial ratings of 1.

The criteria for chronic persistent TD were met by 112 patients (58%). Table 1 gives the association of several baseline characteristics with chronic persistent TD. The following crude (unadjusted) associations were observed: an increase of 20 years in age was associated with 2.1 times the odds of having chronic persistent TD; a three-unit increase in total AIMS score was associated with 1.9 times the odds of having chronic persistent TD; patients exhibiting non-orofacial TD at baseline were associated with 3.6 times the odds of having chronic persistent TD during follow-up; and those with a long duration of TD at baseline (≥31 months) had 3.3 times the odds of having chronic persistent TD as those with a short duration (<15 months). Regarding the longitudinal data (Table 2), the 65 patients with nine or more follow-up visits were 6.1 times more likely to have chronic persistent TD than were the 50 patients with two or three visits. The average dose of neuroleptic medication on the first and last visits varied from 337 mg to 326 mg CPZE in the intermittent group and from 378 mg to 283mg CPZE in the chronic persistent group. Sixty-two (55%) chronic persistent patients experienced a dose reduction from first to last visit, while only 26 (33%) of the intermittent patients experienced a reduction. Patients

Table 1

Estimated crude effects (odds ratios) of selected variables on chronic persistence among TD patients: results of simple (unadjusted) logistic regression analyses

Variable[1]	No. of subjects	Mean or proportion[2]	OR[1]	95% CI of OR	P
Demographic					
Age (increase of 20 years)	192	46.2	2.09	1.35–3.21	<0.001
Sex (male/female)	191	0.393	1.31	0.72–2.35	0.37
Race (white/non-white)	177	0.780	0.61	0.29–1.24	0.18
Lives alone (yes/no)	179	0.190	1.56	0.71–3.44	0.27
Hollingshead Redlich social class	161				
(IV/I–III) (mid/high)		0.385	0.86	0.31–2.29	0.76
(V/I–III) (low/high)		0.460	0.55	0.21–1.44	0.23
Treatment history					
Diagnosis	151				
(schizophrenia/other)		0.550	1.20	0.60–2.91	0.68
(schizoaffective/other)		0.256	0.79	0.30–2.11	0.64
Duration of mental illness: years	109				
13–21/≤12		0.330	0.86	0.34–2.14	0.75
>21/≤12		0.312	1.85	0.70–4.90	0.21
No. of psychiatric admissions	159				
3–5/≤2		0.346	1.17	0.55–2.45	0.68
>5/≤2		0.264	1.06	0.47–2.35	0.88
Neuroleptic medication exposure: months	148				
96–155/≤95		0.324	1.67	0.75–3.70	0.21
>155/≤95		0.324	1.67	0.75–3.70	0.21
Ever on high potency neuroleptics (yes/no)	192	0.781	1.21	0.60–2.40	0.60
Ever on depot neuroleptics (yes/no)	192	0.208	1.09	0.53–2.21	0.81
Movement history					
Baseline AIMS (increase of 3 points)	192	6.5	1.94	1.35–2.77	<0.001
Non-orofacial TD (yes/no)	192	0.542	3.56	1.95–6.51	<0.001
Duration of TD: months	134				
15–30/≤14		0.351	1.78	0.76–4.13	0.18
>30/≤14		0.336	3.33	1.35–8.16	0.009
Dentures (yes/no)	186	0.366	1.65	0.88–3.06	0.11
Follow-up					
No. of visits	192				
4–8/2–3		0.349	4.41	2.09–9.30	<0.001
≥9/2–3		0.339	6.09	2.80–3.24	<0.001
Maximum–minimum dose: CPZ equivalents	188				
21–179/≤20		0.351	1.87	0.92–3.77	0.08
>179/≤20		0.319	2.66	1.26–5.59	0.01
Change in neuroleptic medication (yes/no)	192	0.693	2.32	1.24–4.34	<0.01
Percentage of visits with changes in anti-Parkinsonian agents	192				
1–33/0		0.182	2.10	0.93–4.77	0.08
>33/0		0.214	1.19	0.58–2.44	0.64

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1. For categorical predictors, the compared groups are given in parentheses; the odds ratio (OR) for each comparison is $\exp[\beta]$, where β is the estimated logistic coefficient for that predictor. For continuous predictors, the value in parentheses corresponds to the difference (d) in that variable for which the odds ratio is estimated – i.e., $\mathrm{OR} = \exp[\beta d]$.
2. The mean for continuous variables or the proportion of subjects in the first category for dichotomous variables.

Table 2

Estimated adjusted effects (β and OR) of predictor variables on chronic persistence among TD patients: results of multiple logistic regression analyses[1]

Predictor variable[2]	n	β[2]	s.e.(β)	OR	95% CI of OR	P
Best model						
Age (increase of 20 years)	192	0.0285	0.0128	1.77	1.07– 2.92	0.026
Baseline AIMS (3 points)	192	0.1132	0.0729	1.40	0.92– 2.16	0.120
Non-orofacial TD (yes/no)	192	1.0052	0.3849	2.73	1.29– 5.81	0.009
No. of visits	192					
4–8/2–3		1.3665	0.4119	3.92	1.75– 8.78	<0.001
≥9/2–3		1.5730	0.4273	4.82	2.09–11.14	<0.001
Other variables						
Race (white/non-white)	177	−0.2096	0.4222	0.81	0.35– 1.86	0.620
Sex (female/male)	191	0.1507	0.3707	1.16	0.56– 2.40	0.684
Duration of mental illness: years	109					
13–21/≤12		−0.6814	0.5882	0.93	0.29– 2.96	0.247
>21/≤12		0.1132	0.6896	1.12	0.29– 4.33	0.870
No. of psychiatric admissions	159					
4–6/<3		0.2674	0.4641	1.31	0.53– 3.24	0.564
>6/<3		−0.2330	0.4774	0.79	0.31– 2.02	0.626
Psychiatric diagnosis	151					
schizophrenic/other		0.5197	0.5803	1.68	0.54– 5.24	0.371
schizoaffective/other		−0.0934	0.6061	0.91	0.28– 2.99	0.878
Duration of TD: months	134					
16–31/<15		0.0591	0.5182	1.06	0.38– 2.93	0.909
>31/<15		0.7752	0.5615	2.17	0.72– 6.53	0.167
Percentage of visits with changes in anti-Parkinsonian agents	192					
1–33/0		0.2301	0.4817	1.26	0.49– 3.24	0.633
>33/0		0.5934	0.4463	1.81	0.76– 4.33	0.183
Change in neuroleptic medication (yes/no)	192	0.4257	0.3785	1.53	0.73– 3.21	0.261
Neuroleptic medication exposure: months	148					
97–156/≤96		0.2765	0.5118	1.32	0.48– 3.60	0.589
>156/≤96		0.2797	0.5062	1.32	0.49– 3.57	0.581
Ever on high-potency neuroleptic medication (yes/no)	192	0.2787	0.4226	1.32	0.58– 3.03	0.510
Ever on depot neuroleptic medication (yes/no)	192	−0.0633	0.4365	0.94	0.40– 2.21	0.885
Maximum–minimum dose: CPZE	188					
21–179/≤20		0.1307	0.4278	1.14	0.49– 2.64	0.760
>179/≤20		0.7510	0.4415	2.12	0.89– 5.04	0.089
Average dose: 100 CPZE	192	0.0001	0.0007	1.01	0.88– 1.15	0.896
Dentures (yes/no)	137	0.9654	0.4987	2.63	0.99– 6.98	0.053
Hollingshead Redlich social class	161					
IV/I–III, mid/high		−0.2365	0.5850	0.79	0.25– 2.48	0.686
V/I–III, low/high		−0.3515	0.2879	0.70	0.40– 1.24	0.222
Lives alone (yes/no)	179	0.4439	0.5012	1.56	0.58– 4.16	0.376

1. For categorical predictors, the compared groups are given in parentheses; the odds ratio (OR) for each comparison is exp[β], where β is the estimated logistic coefficient for that predictor. For continuous predictors, the value in parentheses corresponds to the difference (d) in that variable for which the odds ratio is estimated – i.e., OR = exp[β].
2. The effect (β and OR) of each variable is adjusted for all (other) variables listed for the 'best' model.

with the largest difference in maximum and minimum neuroleptic dose (≥179 mg CPZE) had 2.7 times the odds of having chronic persistent TD as compared with those with little change (<20 mg CPZE). Patients with more changes (1–33% of visits) in anti-Parkinsonian agents had 2.1 times the odds of having chronic persistent TD as compared with those with no changes.

The 'best' model for predicting chronic persistent TD, using logistic regression analysis, is listed as the four predictor variables at the top of Table 2. Of the two methodological covariates (total baseline AIMS score and number of visits during the follow-up) which were forced into the model, only number of visits was related to chronic persistent TD. The results of the other predictors in the best model did not change appreciably when we removed baseline AIMS score from the model.

Aside from number of visits, significant ($P<0.05$) predictors of chronic persistent TD were being older and the presence of nonorofacial TD at baseline. Specifically, an increase of 20 years in age was associated with 1.8 times the odds of having chronic persistent TD, and the presence of non-orofacial TD at baseline was associated with 2.7 times the odds of having chronic persistent TD. Other predictors ($P<0.10$) of chronic persistent TD included denture use and a greater difference between maximum and minimum neuroleptic dose during the follow-up period (Table 2).

Because of the exploratory nature of our analysis (i.e. involving multiple comparisons without specific hypotheses), we have also reported the separate effects of all other candidate predictors not included in the best model (Table 2); each of these associations has been adjusted for all predictors in the best model. None of these variables, when added to the model, appreciably altered the results shown for the three significant predictors noted above.

Discussion

Although there was considerable variation in symptom persistence in TD, it remains to be seen whether the intermittent cases ever remit entirely or become chronically persistent. Two reviews (Gardos & Cole, 1983; Casey & Gardos, 1986) have identified likely predictors of TD course: age, duration of exposure to neuroleptics, duration of TD, length of psychosis, anti-Parkinsonian treatments, and an affective diagnosis. In the present study, which is, to our knowledge, the first to consider multiple predictors of TD outcome with adjustment for confounding, the important predictors of persistence were increased age and the presence of non-orofacial movements. We did not find appreciable associations between TD outcome and duration of TD, length of psychosis, change in dose of anti-Parkinsonian agents, or the presence of an affective component to the psychiatric illness when multivariable analysis was employed.

Age is one of the most consistent predictors of TD and its severity (Smith & Baldessarini, 1980). In previous studies of patients from our source population, we have found ageing to be associated with increased prevalence (Morgenstern *et al*, 1987*b*), greater severity (Glazer *et al*, 1988), and poorer outcome following neuroleptic discontinuation (Glazer *et al* (1990). A meta-analysis of five longitudinal studies (Smith & Baldessarini, 1980) suggested a relationship between ageing and persistence of TD. Three previous studies of the course of TD in patients receiving neuroleptic medication found that older patients are less likely to remit or improve than are younger patients (Seeman, 1981; Smith *et al*, 1981; Yassa *et al*, 1984). In the present study, the fact that length of exposure to neuroleptic medication and duration of mental illness did not enter the final logistic model or alter the other findings suggests that ageing is associated with chronic persistence independently of these treatment and illness variables. The pathophysiological mechanism underlying this finding remains to be elucidated, but the leading explanation is loss of dopamine function as a part of the ageing process (Jeste & Wyatt, 1982).

Waddington (1989) has reviewed a number of previous studies that have identified statistically two forms of TD in terms of orofacial and non-orofacial movements. Included in this review was our cross-sectional study of 228 TD cases at baseline of which the 192 cases reported here were included (Glazer *et al*, 1988). We identified statistically two different forms of TD: orofacial and non-orofacial. In addition, multivariable analysis revealed that increased age, schizoaffective or affective diagnosis and living alone predicted severity of orofacial movements, while neuroleptic dose, non-use of other psychiatric medication and living alone predicted the severity of non-orofacial movements. The findings of the present study suggest that non-orofacial movements also have important prognostic implications to the subsequent course of TD. Since we adjusted for total baseline AIMS score, this result does not merely reflect the contribution of non-orofacial movements to the total AIMS score. It will be important to determine whether non-orofacial TD is a distinct aetiological subgroup or an 'end-stage' phenomenon in the course of TD. Our findings suggest the former, because non-orofacial movements predicted chronic persistence independently of ageing; furthermore, this result was not altered when duration of TD, neuroleptic exposure or mental illness was added to the logistic model. Thus, our data suggest that non-orofacial TD is an indicator of poor prognosis.

We found that the number of follow-up visits was strongly and positively related to the probability of being a chronic persistent case of TD. This predictor was included in the best model, not because it is prognostically relevant in a biological sense, but because it reflects a possible source of selection bias when estimating the effects of certain other variables. That is, patients with chronic persistent TD are more likely to continue visiting the TD clinic than are patients with intermittent TD. We also observed, for example, that the effect of changes in dosages decreased substantially when number of visits was added to the model. Thus, the crude effect of dose difference was confounded by number of visits.

It appears that patients with chronic persistent TD, who made more visits to the TD clinic, were also more likely to experience neuroleptic dose changes, possibly in response to their chronic persistent movements. Therefore, we conclude that the crude effect of dose difference on chronic persistence was largely due to bias, and it probably does not reflect a real prognostic factor for TD outcome. On the other hand, our study design does not permit a very complete assessment of this prognostic issue, because we do not know whether specific dose changes occurred before or after specific changes in TD severity.

Finally, denture use was found to be a predictor of chronic persistent TD. Since ill-fitting dentures are included in the differential diagnosis of TD (Granacher, 1981; Jeste & Wyatt, 1982), we always consider this factor in evaluating patients referred to the TD clinic. It is unlikely, therefore, that ill-fitting dentures were confused with TD. To distinguish TD from ill-fitting dentures it is often useful to look for movement exacerbation with the finger-to-thumb exercise or 'elicitation' portion of the AIMS. Movements associated with TD, but not ill-fitting dentures, will usually increase with elicitation. We view the finding with caution because the 95% confidence interval is rather wide (0.99–6.98). Additionally, in our previous studies involving this population (Glazer *et al*, 1984, 1988, 1991; Morgenstern *et al*, 1987*a*,*b*; Glazer & Morgenstern, 1988), denture use was never observed as a predictor of TD, its severity or its course.

This study, although limited to some extent by its retrospective design, suggests that it is useful for clinicians and researchers to consider chronic persistent and intermittent outcome patterns in TD patients who must remain on neuroleptics. Future studies are needed to further clarify these patterns.

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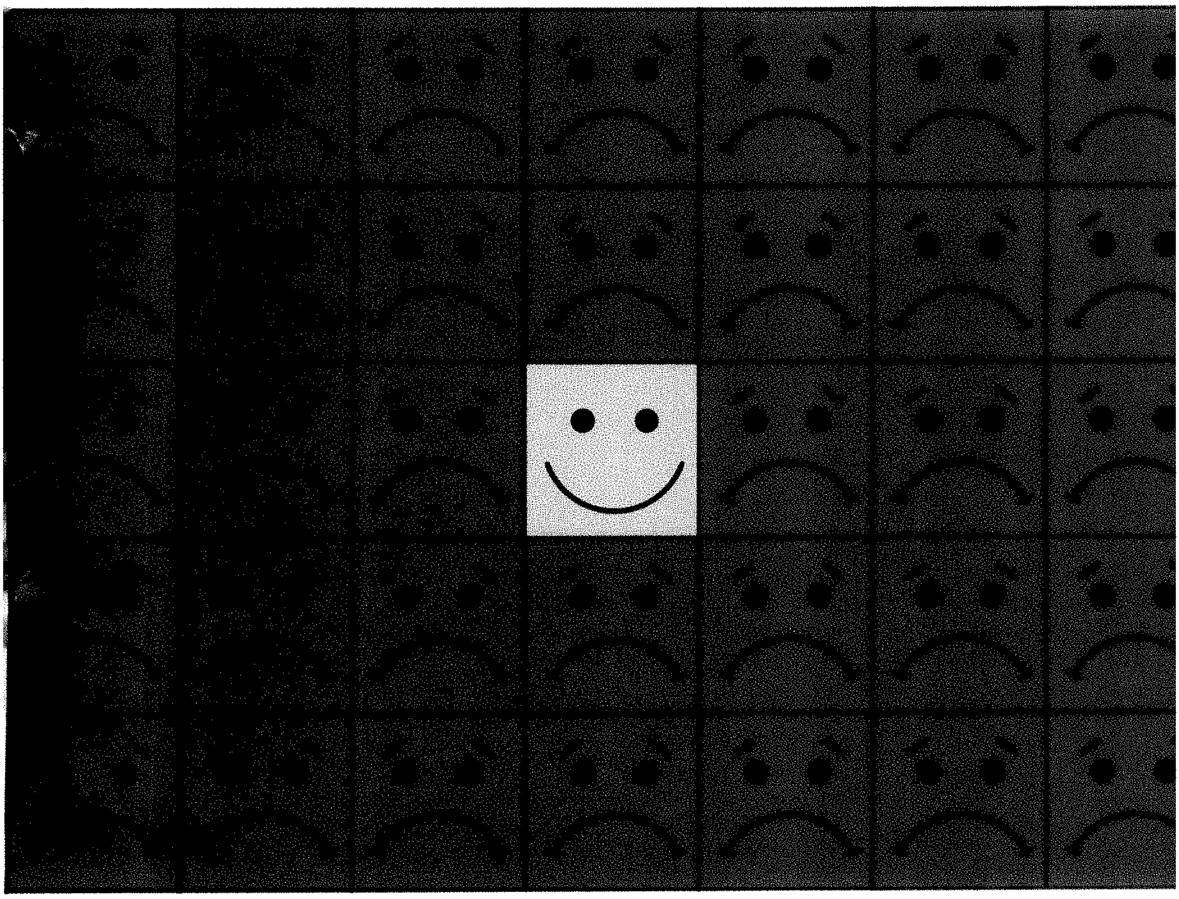

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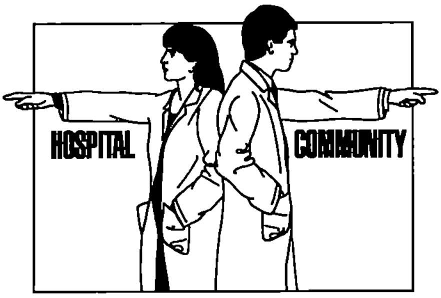

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British Journal of Psychiatry (1991), **158**, 829–833

Adoption and Eating Disorders: A High-Risk Group?

NEIL L. HOLDEN

Between 1975 and 1985, 3.8% of patients referred to the Maudsley Hospital with anorexia and bulimia were adoptees. This exceeds the rate of adoption (1.5%) in the general population matched for year of birth. The 18 adoptees with eating disorders had significantly more associated behavioural disturbance and lower academic achievement than the 18 matched controls, and different precipitating factors.

The association between being adopted and subsequent mental illness in adulthood and late adolescence has received little attention from researchers except those in the field of genetics. Despite the considerable interest in adoption and its recognised association with psychological problems in childhood (Ounsted & Humphrey, 1963; Mackie, 1982), there have been few follow-up studies of children as they move into adulthood. McWhinnie's (1967) retrospective study of the outcome of adoption revealed that 10 out of 58 adopted adults had suffered from mental illness including one with possible anorexia nervosa. Whether those who have been adopted are at greater risk of all or specific mental illness has not been adequately answered, although Wieder (1977) found a 15–30% incidence of adoptees in the psychiatric population compared with 2% of the general population.

This study investigates the relationship of adoption to eating disorders. Fry & Crisp (1989) reported a case of anorexia nervosa in a male adoptee and discussed psychodynamic issues associated with this case. However, they considered the association of adoption and eating disorder to be rare, as judged by the sparseness of case reports in the literature. If it can be shown that more patients with eating disorder than expected have been adopted, then this raises questions as to why there should be such an association, and how such patients differ in their psychopathology from typical patients with eating disorders. The possibility that such a study might contribute to the knowledge of the genetics of eating disorders must also be considered. Holland *et al* (1984, 1988) studied twins to demonstrate a genetic contribution to the aetiology of eating disorders. Cantwell *et al* (1977) and Winokur *et al* (1980) for anorexia nervosa, and Hudson *et al* (1982, 1983) for bulimia, suggested a genetic relationship to affective disorders. This study reviews the family history of a series of adoptees with eating disorders in further consideration of these genetic theories.

Method

By examining the records of all patients seen at the eating disorders unit of the Maudsley Hospital between 1979 and 1985, those recorded as having been adopted at birth were identified. Eighteen patients (3.8%) out of a total of 470 (230 bulimia nervosa, 240 anorexia nervosa) were adoptees. Nine of the adoptees were diagnosed with anorexia nervosa (3.75% total anorexic cases) and nine with bulimia nervosa (3.9% of total bulimia cases). Each adopted patient was matched with the next patient of the same sex and diagnosis referred to the eating disorders unit, to form a non-adopted control group.

Mean population matched weight (MPMW) for each patient was derived from the *Statistical Bulletin* of the Metropolitan Life Insurance Company (1983). The patients and their fathers were allocated to socio-economic groups using the *Classificaton of Occupations* (Office of Population Census and Surveys, 1980). Diagnoses for anorexia and bulimia nervosa were made according to the criteria of DSM–III–R (American Psychiatric Association, 1987). Depression was recorded when the psychiatrist performing the mental state examination had noted depressed mood but does not necessarily imply the presence of a depressive disorder. Demographic and clinical characteristics of the adopted patients were compared with the controls using paired t-tests and χ^2 tests.

Results

Eighteen adopted patients (4 men, 14 women) (mean height 167 cm, s.d. 6.0, range 154–178 cm) were matched to 18 control patients (mean height 166 cm, s.d. 8.7, range 154–183 cm). The mean pre-morbid weight of the adopted group, expressed as percentages of the mean population matched weight was 96% (s.d. 10.1, range 78–115%) while that of the control group was 93% (s.d. 8.8, range 81–109%). The mean ages of onset of the adopted and control groups were 16.4 years (s.d. 1.8, range 14–20 years) and 17.5 years (s.d. 2.9, range 14–24 years) respectively. By the above variables the groups are well matched.

The clinical and demographic data of the two groups are shown in Table 1, and present a typical picture of eating disorders broadly comparable with previously described series of those with bulimia nervosa (Fairburn & Cooper, 1984) and anorexia nervosa (Crisp *et al*, 1980). The clinical symptoms of the two groups were similar, including the

Table 1
Clinical and demographic features of the patients

Height: cm	MPMW[1] kg	% MPMW				Age at onset: years	Duration: months	Binges	Vomiting	Laxatives	Excessive exercise[4]	Amenorrhoea: months	Diagnosis	Education beyond 16 years	Occupation	
		Pre-morbid	Current	Maximum[2]	Minimum[3]										Patient	Father
Adopted																
166	61	98	100	107	79	18	42	+	+	+	-	42	BN	+	Student	Director
168	66	102	76	102	76	19	24	-	+	+	+	NA[5]	AN	-	Nurse	Electrician
178	71	107	86	107	80	16	4	-	-	-	+	NA[5]	AN	-	Warehouseman	Carpenter
168	62	103	79	118	61	15	25	-	-	+	-	25	AN	-	Nurse	Director
154	55	87	58	93	58	13	10	-	-	-	-	8	AN	-	Scholar	Labourer
163	60	95	90	95	85	19	36	+	+	-	-	-	BN	+	Sales	Bank manager
169	63	106	71	106	63	16	4	-	-	-	-	4	AN	-	Clerk	Shop owner
173	69	97	84	97	74	15	18	+	+	-	-	NA[5]	BN	-	Student	Manager
175	66	115	89	115	67	20	35	+	+	+	+	Irregular	BN	+	Student	Teacher
166	61	93	89	95	67	16	108	+	+	+	-	-	BN	-	Secretary	Executive
160	58	110	93	124	59	14	156	+	+	+	-	-	BN	-	Secretary	Musician
168	62	82	95	95	56	15	84	+	+	-	-	36	BN	-	Receptionist	Engineer
172	64	102	86	102	70	17	36	+	+	-	-	30	BN	-	Shop Assistant	Engineer
174	69	78	70	90	55	16	15	-	-	-	+	NA[5]	AN	-	Waiter	Hairdresser
170	63	90	81	90	63	16	7	-	-	-	-	6	AN	+	Student	Engineer
165	61	89	128	141	48	15	20	+	+	+	+	19	BN	-	Unemployed	Manager
163	60	87	67	87	63	18	72	-	-	-	+	84	AN	-	Secretary	Clerk
160	58	88	76	88	66	18	6	-	+	+	-	6	AN	-	Clerk	Executive
Controls																
168	62	84	94	94	84	24	8	+	+	-	-	-	BN	+	Loc.Gov.Off.	Engineer
175	70	86	73	86	73	16	9	-	-	-	-	NA[5]	AN	+	Scholar	Postmen
171	68	97	63	97	63	16	12	-	-	-	+	NA[5]	AN	+	Scholar	Technologist
165	61	93	59	93	59	16	30	-	-	+	-	30	AN	+	Student	Teacher
155	55	93	60	93	58	22	16	-	-	-	+	6	AN	-	Secretary	Architect
169	63	105	94	105	83	18	60	+	+	+	-	9	BN	+	Nurse	Clockmaker
151	54	81	67	81	57	14	30	+	+	+	-	30	AN	-	Scholar	Manager
183	74	109	99	109	74	18	6	+	-	-	+	NA[5]	BN	+	Student	Farmer
157	56	107	113	141	95	15	120	+	+	+	-	-	BN	-	Secretary	Bank manager
165	61	98	85	102	67	17	48	+	+	-	-	18	BN	+	Secretary	Solicitor
157	56	98	111	113	88	18	36	+	+	-	-	-	BN	+	Student	Lecturer
164	60	90	83	90	80	18	50	+	+	+	-	50	BN	+	Student	Driver
167	62	81	113	118	81	17	48	+	+	+	-	Irregular	BN	+	Manager	Teacher
175	70	91	59	91	59	14	7	+	-	+	+	NA[5]	AN	+	Scholar	Care Asst.
154	55	84	49	84	49	15	8	-	-	-	-	8	AN	-	Scholar	Bricklayer
168	62	102	97	103	71	15	45	+	+	+	-	12	BN	-	Nurse	Computing
175	66	86	62	86	56	21	5	-	+	-	+	5	AN	+	Student	Teacher
173	65	88	72	98	72	22	36	+	+	+	-	36	AN	+	Teacher	Teacher

1. MPMW = Mean Population Matched Weight (Metropolitan Life Insurance Co. 1983).
2. Max Wt = Maximum weight ever as percentage of MPMW.
3. Min Wt = Minimum weight ever as percentage of MPMW.
4. AN = anorexia nervosa, BN = bulimia nervosa.
5. Male.

amount of bulimic behaviour, depressive and obsessional symptoms and the presence of amenorrhoea in the females. The mean duration before presentation was 39 months in the adopted group (s.d. 41, range 4–156 months) and 32 months in the control group (s.d. 28.6, range 5–120 months), a non-significant difference. The patient's stated age of menarche/puberty and source of referral of the two groups was similar.

Some differences were observed between the two groups. Childhood obesity, as perceived by the patients themselves, was reported significantly more often in the adopted group than the control group ($P<0.05$). The level of educational achievement of the adopted group was significantly lower than in the control group ($P<0.05$). This finding was reflected in the trend ($P<0.06$) towards a lower socio-economic level of patients' employment in the adopted group. There was no difference in the socio-economic class of the parents of the two groups.

Six of the adopted group had carried out parasuicidal acts and six had had problems with substance abuse compared with two and one of the control group respectively. Although the patients with such behaviour overlapped, 11 adopted patients had carried out parasuicide, substance abuse or theft, compared with three control patients ($P<0.05$). There was a trend ($P<0.06$) towards the adopted patients having more emotional and conduct disorders of childhood compared with controls (11 adopted, 5 controls). There was no difference in the previous sexual experience and adjustment of the two groups.

There appear to be few differences in family history of mental illness in the adopting families compared with the controls. The adopting families were understandably smaller with only 16 siblings (3 female, 13 male) compared with 34 siblings (19 female, 15 male) in the controls. Six of the adopting families had a history of mental illness in first-degree relatives compared with eight of the control families. Of the six adopting families with such histories, six parents, but no siblings, had histories of affective disorders (one complicated by alcohol abuse). One brother had a childhood conduct disorder. Eight first-degree relatives of the control group had histories of affective disorder, seven being parents. Four first-degree relatives of the adoptees had 'weight problems' – two with obesity and two with persistent dieting. In the control group there were two first-degree relatives with obesity, two with bulimia nervosa and one with anorexia nervosa. None of these differences reached statistical significance. There was insufficient information available on the natural families of the adopted patients to draw any conclusions, and further investigation of biological origin was not possible for ethical reasons. There were few differences between the proportions of the two groups that had major disharmony or disruption of family structures. In five families of both groups the parents had severe marital disharmony, being separated or divorced. Two of the adopting sets of parents had unconsummated marriages. Three of the control cases had death or severe physical illness in one parent compared with none of the adopted families.

Eight of the adopted patients felt that their adopted status played a role in their illness and general psychopathology. In some of these cases the adoption had been revealed during arguments with their parents. Social dieting was quoted as the cause for the initial disturbance of eating in six of the control patients but in none of the adopted patients ($P<0.05$). Infection or other physical illness was stated as a precipitant in two of the controls and one adopted patient, while problems with girlfriend or boyfriend relationships was quoted in three controls and four adoptees. Social, work and examination pressure was blamed in four or five cases in both groups. Teasing or bullying at school was a claimed precipitant in three of the adopted patients but none of the controls.

All the adopted patients had been adopted between birth and nine months. Where information was available, it was known that adoption was arranged because of illegitimate status (six cases).

Discussion

The Registrar General's figures (Home Office Research Studies, 1972) for the proportion of adoptions (by others as opposed to parents) per 100 live births are available for each year of birth. The figures vary from 1.2% in 1958 to 2.0% in 1968. The average for the duration of this study was estimated at 1.5% by matching the adoptees' years of birth to the official national statistics. If it can be assumed that these national figures reflect the true rate of adoption for the catchment area around London and the South-East from where these patients are drawn, then there is a significant over-representation of adopted patients (3.8%) in the overall number of referrals. Since adopted individuals are not certain to report this fact, and interviewers may not have inquired directly, this is likely to be an underestimate. This over-representation of adoptees reflects the findings of excess psychological morbidity in adopted children (Ounsted & Humphrey, 1963) and consideration needs to be given as to why this is occurring.

In this study, the adopted and non-adopted cases of eating disorders are very similar on most parameters and the groups are well matched. Some differences have been shown, however. Childhood obesity is more often reported in the adopted group. It might be postulated that this is true obesity caused by overfeeding by anxious adoptive parents. Alternatively, since this is a subjective report rather than an objective measure, it may reflect the early self-perception of these patients in comparison with either biologically different parents or more self-assured peers. These possibilities need to be considered in the light of an adoption study of fatness (Price *et al*, 1987) which found that there was a strong relationship between the fatness of the biological mothers and that of the adopted offspring, but also that disturbance in the adoptive home predicted fatness among the adoptees.

Another significant difference was the lower level of educational achievement of the adopted patients. This disparity between observed and expected achievement may have aetiological significance through the adopted patients failing to achieve the expectations of the adopting parents. This may increase the sense of failure on the part of the adoptee, lowering self-esteem and creating a poor self-image. The family characteristics of bulimics were investigated by Johnson & Flach (1985), who showed that higher achievement expectations were associated with the severity of bulimic symptoms.

There is evidence that the adopted group are more behaviourally disturbed with significantly more parasuicidal acts, substance abuse or theft. This self-destructive and antisocial behaviour may reflect aspects of the psychopathology of adolescence magnified by the adopted state; it is possible that efforts towards independence against adopting parents are potentially more difficult and escalate into frank rebellion and maladaptive behaviour.

In their studies of twins, Holland *et al* (1984, 1988) estimated that up to 80% of the variance in liability to anorexia nervosa was genetic, although they could not rule out the role of environmental induction. If eating disorders are genetically determined, it would be expected that the adopting families would be less often affected by such disorders than controls. This study revealed three cases of eating disorders affecting first-degree relatives of the control group, but none in the adopted group. As this fails to reach statistical significance, no conclusions can be drawn, but it might indicate some support for a genetic effect, however mediated.

It has been suggested (Cantwell *et al*, 1977; Winokur *et al*, 1980; Hudson *et al*, 1982, 1983) that there is a strong association between eating disorders and a family history of affective disorders. In the adopted and control groups in this study 11.5% and 11.4% of first-degree relatives respectively, had affective disorders lending no support to any genetic basis for such a link. These ratios are similar to those found by Holland *et al* (1984), but are less than the 17.5% found by Hudson *et al* (1983) for bulimia (DSM–III; American Psychiatric Association, 1980), and the 22% found by Winokur *et al* (1980) for anorexia nervosa. Cadoret *et al* (1985), in an adoption study of depression, found that environmental factors occurring with adoptees before the age of 18 years predisposed to depression, and biological background was shown to be not significantly associated with depression.

The question remains as to whether the environment of adoption is psychologically damaging. Eight of the adopted patients in this study felt that their adoption had played a role in their illness, both in its genesis and in the issues which they faced over eating. Most of the adopting parents would have been subjected to vetting for mental and physical illness by the adoption agencies, so it is surprising that these parents are still found to have a high degree of psychopathology both with frank affective illnesses and behaviour such as marital disharmony and non-consummation of marriage. Some of these problems may relate directly to the need for the adoption (infertility, for example), but others may be rooted in the stresses created by the adoption of a child. The finding that social dieting is significantly less common as a precipitant in the adopted group may reflect the abundance of problems for parents and child during the adolescent phase of adoption.

The genetic characteristics inherited from the natural parents of the adopted group could not be studied, as insufficient information was available and further investigations would have been unethical. However, it is possible that mental illness in the natural parents may have predisposed the adoptees to the excess of behavioural problems.

Sorosky *et al* (1975) reviewed the nature of identity conflicts in adoptees and summarised the problems in four categories: disturbances in early object relations, complications in the resolution of the 'Oedipal' bond, prolongation of the 'family romance' fantasy, and genealogical bewilderment. These are discussed in relation to eating disorders by Fry & Crisp (1989). Genealogical bewilderment in children with uncertain knowledge of their natural parents was first described by Wellisch (1952). Its role in identity and self-image has been discussed by Sants (1964). He argued that lack of knowledge about who they are in a genealogical sense distorts the development of self-image and self-esteem. If correct, this theory would help explain the excess morbidity for eating disorders in adoptees.

This study, being retrospective and of limited size, needs replication, as results may have occurred by chance alone. More research is needed into adoption and its effects on both parents and child in adolescence and adulthood. Such studies should be extended into the effects of adoption within other psychiatric diagnoses and into subclinical psychopathology. Such research is essential if adoption is to be relied upon in studies of the genetics of mental illness.

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The Current Literature

Is Schizophrenia Disappearing?

JOHN M. EAGLES

"The incidence of schizophrenia is regarded as being similar between different cultures and times. However, several studies, mostly based on first-admission rates, have suggested that the incidence has declined over the past 10–15 years. Data from England and Wales for 1952–86 have been examined: there has been a substantial decrease, beginning in the mid-1960s, in the incidence of schizophrenia."

The summary quoted above is from an article by Der *et al* (1990). John Eagles was invited to comment on the study.

Fluctuations over time in the incidence of a disease can yield important information about its aetiology. In the case of schizophrenia, a significant decline in incidence would suggest strongly that there has been a major change in one or more environmental factors which cause, or lead to the expression of, the disease. The present study follows others which have shown a major decline over the last 20 years in the rates of schizophrenia diagnosis among new psychiatric in-patients in Scotland (Eagles & Whalley, 1985), Denmark (Munk-Jorgensen, 1986; Munk-Jorgensen & Jorgensen, 1986) and New Zealand (Joyce, 1987).

Mr Der and his colleagues have not escaped some of the complexities of method inherent in studies of this nature. They acknowledge that their data on schizophrenic first admissions to English and Welsh hospitals between 1952 and 1970 are somewhat patchy as a result of incomplete data and changes in methods of data collection. In addition, they had to make adjustments to the figures of 'first admissions' between 1964 and 1969, as a result of imprecision at that time in the distinction between a first admission and a readmission. Their first-admission rates are calculated, it appears, on the basis of the total population of England and Wales for each of the years studied. One can quibble with this method on the basis that the majority of schizophrenics will be admitted to hospital for the first time between their late teens and late thirties, and that fluctuations in the age structure of the population (notably the 'baby boom' in the 1960s, and increasing longevity) could have a significant effect on rates calculated in this manner, particularly when the period of investigation spans over 30 years. Age-standardised rates would have yielded a more precise picture.

However, the magnitude of the decline in schizophrenic first admissions (around 50%) almost certainly indicates that these problems of method do not constitute factors of major importance. This decline took place between the mid-1960s and the mid-1980s with a sharper decline in men than in women, but without much difference in magnitude of overall decline between the sexes.

The authors address alternatives to the explanation that these data indicate a genuine decline in the incidence of schizophrenia. They note that there has been a consistent fall in first admissions with affective psychosis and with neurotic disorders, while the rates for 'other psychoses' remained stable. It is implausible, therefore, that schizophrenics were being 'rediagnosed' into these categories. In this context, it is noteworthy that the decline in schizophrenic first admissions commenced in the mid-1960s, especially since studies in other countries have not investigated years before 1969. One possible explanation for a decline in diagnoses of schizophrenia after 1969 was the introduction of lithium carbonate, after an increase in such diagnoses following the introduction of the neuroleptics. Such a pattern has been suggested in the USA (Baldessarini, 1970), but would not fit the data in this study since lithium was not used on a significant scale in the UK until five years after the start of the decline in schizophrenic diagnoses.

The other major alternative explanation to that of a fall in incidence of schizophrenia is that the data reflect the movement towards community care and a resultant, increasing tendency to treat schizophrenics without their ever being admitted to hospital. They note that while schizophrenics constituted 21% of first admissions in 1952, this proportion had fallen to 9% by 1986. It is exceedingly unlikely that the trend towards treatment of schizophrenics in the community could have outstripped that tendency among patients with milder psychiatric disorders. The authors also note our findings in Aberdeen, where first contacts with psychiatric services (as opposed to first admissions) had fallen by over 50% since 1969 (Eagles *et al*, 1988).

The authors conclude, correctly in my view, that the incidence of schizophrenia in England and Wales has fallen significantly since the mid-1960s. One must therefore hypothesise that there has been a major change in one or more aetiological factors over that period. In this context, Fig. 3 of their paper (reproduced in Fig. 1) is perhaps particularly revealing. This figure contrasts the ages at the time of first admissions in 1970 and in 1981, showing rates for males and females. It shows that there was little change for patients aged 55 and over, and the authors hypothesise that this may reflect a stability in rates of admissions with paranoia, since these were included among the schizophrenic data. However, in younger patients, all other age groups in both sexes appeared to show a relatively consistent fall in incidence between 1970 and 1981.

Hypotheses of environmental precipitants of schizophrenia have tended to centre upon perinatal factors, with some evidence for the role of prenatal infection and growing evidence for the importance of obstetric complications. However, if changes in such perinatal factors were solely responsible for the declining incidence of schizophrenia, then we would be witnessing its selective fall among younger patients.

The evidence from this study, therefore, suggests that one or more current environmental risk factors have declined in frequency or virulence between the 1960s and the 1980s. Any such factor would be likely to affect the expression of a constitutional predisposition towards schizophrenia, be that predisposition genetic, or acquired in the prenatal period. Perhaps the most plausible possibilities among such environmental precipitants would be those infectious diseases which declined markedly in prevalence and/or incidence between the 1960s and the 1980s, either as a result of immunisation programmes or increased herd immunity. Rubella, measles, poliomyelitis, whooping cough and diphtheria all fall into this category. It is of note that rates of infection in populations in the USA with diphtheria (Watson *et al*, 1984), measles and poliomyelitis (Torrey *et al*, 1988), in the prenatal period have been linked to rates of subsequent schizophrenia.

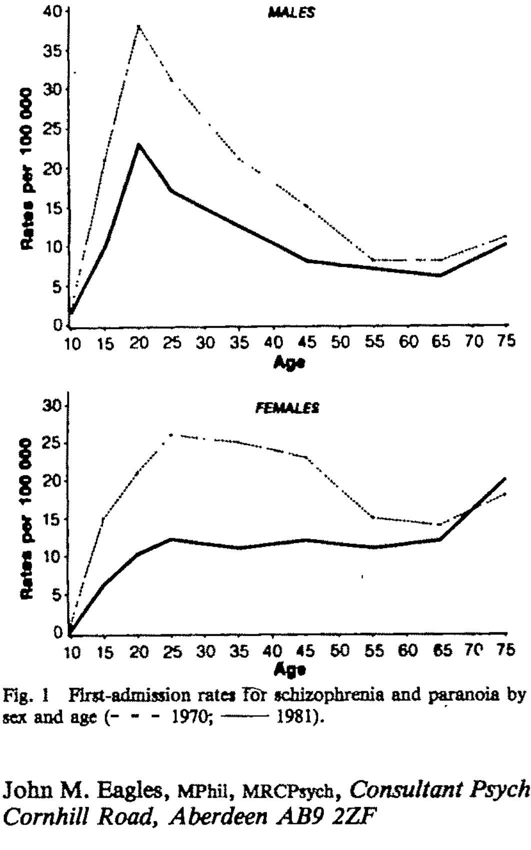

Fig. 1 First-admission rates for schizophrenia and paranoia by sex and age (- - - 1970; —— 1981).

The authors conclude their article by advocating that comparisons be made of individuals diagnosed schizophrenic within the last three decades, using standardised diagnostic criteria for schizophrenia in order to determine what part has been played, if any, by changing diagnostic practices in producing their findings. It seems necessary, also, to investigate further the social and demographic characteristics of the specific population which has shown the greatest decline in incidence of schizophrenia, since this may yield valuable information about the aetiology of the disorder.

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Exposure Therapy for Post-traumatic Stress Disorder

Four Case Studies

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Four cases of PTSD, and their treatment, are described. Symptoms responded differently to two behavioural approaches. *In-vivo* exposure was effective for phobic anxiety while imaginal exposure improved dysphoria and some phobic symptoms. Audio-taped imaginal exposure may be important as part of treatment.

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Post-traumatic stress disorder (PTSD) was first included in the DSM–III diagnostic manual in 1980 (American Psychiatric Association), although the concept of a stress-generated neurotic condition is much older. The diagnosis of PTSD requires several conditions to be met including traumatic genesis of the problem, heightened arousal, avoidance, disassociative symptoms and re-experiencing symptoms.

Post-traumatic stress disorder has since been the subject of much research. Descriptive studies (e.g. Keane *et al*, 1987) have validated the diagnostic criteria. Other studies (e.g. Foy & Card, 1987) have investigated which factors predict development of PTSD, including: extent and nature of the trauma experienced, role of personality, past psychiatric illness, previous life events, degree of social support, and previous coping styles.

The disorder has been treated with techniques derived from many perspectives including psychodynamic, behavioural, and biological. However, there are certain core components which are common to all treatments. Friedman (1988) makes the point that:

> "pharmacotherapy alone is rarely sufficient to provide complete remission of PTSD. Symptom relief provided by medication enables the patient to participate more thoroughly in individual, behavioural or group psychotherapy."

The majority of reports of behavioural or dynamic psychotherapy include descriptions of procedures where imagery is used to treat PTSD. This literature is summarised by Fairbank & Nicholson (1987) who conclude that:

> "direct therapeutic exposure to the memories of trauma emerged as the treatment technique common to all three theoretical models."

The precise form of imagery used differs between and within the different models.

Behavioural models of PTSD

The avoidance of situations and objects directly associated with the trauma and marked physiological arousal in the presence of feared stimuli are major PTSD symptoms. A similar picture is seen in specific phobias. However, PTSD has certain dissociative symptoms not present in phobias such as psychogenic amnesia, re-experiencing symptoms such as flashbacks and nightmares, and heightened levels of general arousal.

The model of PTSD described by Foy *et al* (1987) considers the symptoms to be a conditioned response to a traumatic event. Everyday objects and situations become associated with the traumatic event. These conditioned stimuli then provoke the same response as the original trauma. The response persists for a number of reasons, including the sufferer's avoidance of stimuli associated with recall of the traumatic memory and avoidance of the memory. This reduces the opportunity for exposure to the emotions provoked by the memory, leading to continued symptoms.

Although PTSD, by definition, must involve exposure to an aversive event, most phobics do not report such an experience at the start of their problems. More recent explanations for the development, selectivity and appearance of phobias at certain ages have included Gray's (1987) ideas on maturation and innateness. If the route of acquisition of specific phobias is different from those fears acquired traumatically then the outcome of treatments successfully used to treat phobias may be less confidently predicted in PTSD.

Graded, prolonged and repeated *in-vivo* exposure to feared cues has been shown to be the most reliable way of eliminating phobias (Marks, 1981). It is at first attractive to use such techniques with an apparently similar condition such as PTSD. However, should the differences between PTSD and phobias outlined above outweigh the similarities then they may not be appropriate. Alternatively, *in-vivo* exposure may not be sufficient for the treatment of PTSD. Although *in-vivo* exposure is generally regarded as more effective than imaginal exposure with phobics and obsessives (e.g. Marks, 1981) there are some situations where real-life exposure is not practical nor possible and imaginal exposure is then used.

As previously noted, imagery has been reported as central to most PTSD treatment programmes. Behavioural applications of imagery include systematic desensitisation (Wolpe, 1958) (involving repeatedly pairing a feared stimulus in imagination with a competitive and incompatible emotional state, such as relaxation), 'implosive' therapy (Stampfl & Levis, 1967), guided fantasy and 'imaginal' exposure. The key component of all imaginal behavioural techniques is that the patient experiences anxiety in imagination, holding the image until he feels comfortable and no longer anxious.

Much of the literature on imaginal behavioural techniques in PTSD includes a relaxation component (e.g. Saigh, 1986). With phobics, relaxation increases the time taken for therapy to be completed and has been shown to be unnecessary for clinical improvement (Gillan & Rachman, 1974). Some of the PTSD studies using relaxation also include implosive or dynamic themes.

Four cases are presented where both imaginal and *in-vivo* exposure were used to treat PTSD. Imaginal exposure does not involve relaxation or dynamic cue presentation. Imaginal cues are re-creations of the person's memories of the original traumatic incident. Imaginal exposure was audio-taped to facilitate imaginal exposure homework.

Treatment method

A typical imaginal treatment session lasted 90 minutes, of which 60 minutes was exposure. The patients were asked to imagine and recount their traumatic experience in the first person, present tense, i.e. as if it were actually happening in the treatment session. Therapist intervention was minimal except to encourage the patient to hold difficult scenes in their imagination until they became less distressed. The patient was asked to listen to the audio-tape of the session at least four times a week for one hour at home and to imagine the scene, thus repeating the treatment session at home. All four patients complied with this instruction. New tapes were generated from each subsequent treatment session.

Table 1
Mean patient scores on outcome measures

	Fear Questionnaire	Dysphoria	Problem rating	Target rating	Social adjustment	Beck Depression Inventory
Pre-therapy	46	27.5	7.5	7	18.5	18.7
Post-therapy	26.5	7.8	2.8	0.5	6.8	7
Follow-up[1]	8.7	5	1.3	1	1.3	3.5

1. Follow-up data available for three patients only.

Outcomes were measured by standard measures of mood (Beck Depression Inventory (BDI), Beck *et al*, 1974), anxiety (Fear Questionnaire (FQ), Marks & Mathews, 1979), social adjustment (Marks, 1986) and with self-report of behavioural change. Outcome measures are summarised in Table 1.

Case reports

Case 1

B, a 47-year-old electrician working in a pharmaceutical factory, presented with a phobia of electrical machinery, particularly large high-voltage contactor panels. This was preventing him from doing his job and his future with the company was in jeopardy.

His problems began in January 1984 when he awoke one morning with a severe headache. From that time his headaches were severe, frequent and extremely debilitating. An extensive neurologist's examination could find nothing to explain his condition. The only other symptom was an occasional shakiness. He took numerous days off work because of headaches and used excessive amounts of pain killers.

In September 1986, two and a half years after the headaches began, he was sleeping at work during a tea break when a colleague took a photograph of him using a flashgun. He awoke with a start and had an intrusive image ('flashback') of an accident at work nearly seven years earlier while he was mending a contactor panel. There had been an explosion in the panel which had burnt his face and hair, temporarily blinding him. Subsequent explosions in the panel were particularly frightening as he could not see to get away. Following the flashback he started to have frequent, vivid nightmares of the incident, during which he could smell his burning flesh. He became convinced that the explosion was the source of his headaches and was referred to a psychiatrist, who performed abreaction on him three months later.

After the abreaction his headaches vanished, but he became acutely fearful of the electrical panels. This phobic anxiety became worse until he was unable to do any of his normal duties. Two months later his headaches returned at a frequency of two per week. Nightmares were still a feature, as was excessive use of pain killers. He was moderately depressed, felt the future was hopeless and found it difficult to make decisions. At this point an urgent referral for behaviour therapy was made to try to resolve his phobic anxiety.

The first ten weeks of treatment comprised *in-vivo* exposure to the electrical contactor panels, during which he performed standard examination procedures on the panels. The sessions were graded over the ten weeks gradually achieving an increasing similarity to the procedure which had led to his initial trauma. His phobic anxiety was eliminated by this approach but his headaches increased in frequency and intensity, so that for the last four weeks of *in-vivo* exposure they were occurring constantly.

A one-hour session of imaginal exposure to the actual explosion then took place, consisting of two half-hour presentations of the image. During the imaginal exposure B reported experiencing the smell of his burning flesh. The session was audio-taped and this was used for repeating the imaginal exposure at home four times weekly for the next two weeks. Three days after the first session of imaginal exposure his headaches reduced to a frequency of two per week.

At discharge (week 17, following 11 treatment sessions), B showed reductions in anxiety and depression to minimal levels on the BDI and the Dysphoria subscale of the FQ. Improvement continued at six-month follow-up. His headaches had stabilised at one per week, lasting only a couple of hours and required no prescribed medication for their control. He was able to resume his duties as an electrician and his job was secure.

Case 2

G, a 29-year-old police constable, presented with fear and avoidance of leaving the police station. He felt extreme panic when he attempted to do this, suffering palpitations, nausea and hyperventilation. His problems were preventing him from working. He had no past psychiatric history or history of drug or alcohol abuse. He described himself as a perfectionist, worrying at any time if he was unable to give his best to his job.

Onset of this problem was during an incident at work when he was threatened by two youths while reprimanding a member of the public for a traffic offence. During this confrontation he had a 'flashback' of an incident two years earlier when he had been hit while arresting a shoplifter. As a consequence of this flashback he became so paralysed with fear that he could not even call for help on his radio and had to back down from the confrontation.

Treatment took eight sessions. The first session, lasting one hour, consisted of imaginal exposure to the initial incident when he had been hit. This session was audio-taped and he used the tape for daily imaginal exposure at home. After three weeks, when his anxiety at imagining the scene had reduced by 75%, he undertook *in-vivo* exposure to normal police activities by returning to work. He graded the work he had to do and avoided conflict situations for the first three weeks back at work. He then re-started all normal police work.

At discharge, his FQ score had reduced from 48 to 18 and dysphoria from 35 to 6. BDI score reduced from 21 to 7. These improvements persisted to three-month follow-up and he continued to work as a policeman without any further difficulties.

Case 3

E, a 41-year-old woman, was attending a psychiatric day hospital after general practitioner (GP) referral for agoraphobia and panic. She was severely handicapped, could not walk or shop alone, could not travel on buses and avoided paying for goods or going into a bank. She feared that she would get attacked, particularly when men were present. She was also generally anxious and depressed.

Her problems started two and a half years earlier after she was robbed by two armed men while working as a petrol station attendant. Although not physically injured, she was repeatedly threatened with an axe and an iron bar. Following the attack she was unable to return to work, had frequent nightmares related to the incident and many intrusive 'flashback' experiences. One of these occurred three days after the incident when she 'saw' her attackers leaping out of a cupboard at home. She had not been able to open the cupboard again since that day.

There was no previous psychiatric history and nothing of note in her family or personal histories. During eight months at the day hospital she was treated with major and minor tranquillisers and an antidepressant, and took part in anxiety management groups, relaxation classes and an *in-vivo* exposure programme. Although drugs were helpful for her sleep problems, none of the above approaches alleviated her PTSD symptoms.

She then received seven sessions of specialist behaviour therapy, consisting of ten hours in total, three and a half of which were therapist-aided. Her assessment showed continuing high levels of phobic anxiety, dysphoria and general handicap, and moderate depression. The first three sessions consisted of one hour of imaginal exposure to the attack. The sessions were audio-taped and E repeated the exposure daily with the aid of the tape. At first she was accompanied by nursing staff, then later her husband, and finally alone. After four weeks of this approach her anxiety while imagining or thinking about the scene had reduced by 50%. Mid-treatment measures showed 50% reductions in dysphoria and depression scores but little reduction in phobic anxiety.

In-vivo exposure exercises were re-started and this time were quickly successful. She was gradually able to enter her feared situations and could open her cupboard for the first time since the attack. She can now enter most normal social situations, pay for goods in shops, and travel on buses. Flashbacks and nightmares remain but at a reduced frequency and intensity. Depression and dysphoria were reduced still further at discharge but follow-up data are not available.

Case 4

K, a 32-year-old policeman, was referred for behaviour therapy for management of explosive outbursts of anger in crowded situations. In these situations he would feel nauseous, sweaty, increasingly tense and would physically push his way out of the crowd to freedom. He presented with moderate depression with initial insomnia, nightmares and increased irritability. Because of his problem he had been off work for 12 months. The problem started four years earlier when he had been crushed in a crowd control incident that had left several people dead; he had lost consciousness before being pulled to safety. Since the incident, treatment had consisted of several lengthy stays in police convalescent homes and he had recently been prescribed thioridazine (50 mg nocte).

Treatment was by four sessions of therapist-assisted imaginal exposure to the initial incident with audio-tapes for homework. At this point he showed marked reductions in nightmares, his mood improved significantly and he became much less irritable. He felt able to commence a programme of *in-vivo* exposure, which previously he had refused to contemplate. *In-vivo* exposure was homework-based with his wife as a co-therapist and consisted of graded exposure to crowded situations. It was also possible to stop his medication at this point.

At discharge, five weeks later, he was back in uniform and able to carry out all normal police duties. On a range of outcome measures his improvement was rated at over 80%. These gains were maintained at six-month follow-up.

Discussion

Four cases of long-standing and severely debilitating PTSD were successfully treated with a combination of *in-vivo* and imaginal exposure. Therapy was swift and effective, leading to resolution of all major PTSD symptoms. The use of audio-tapes for imaginal exposure homework greatly increased the amount of exposure possible without requiring further therapist time. Self-exposure has been shown to be crucial for the effectiveness of *in-vivo* exposure (McDonald *et al*, 1979). Audio-tapes allow the same principles to be applied to imaginal exposure, resulting in more rapid treatment gains for our patients. Relaxation was not necessary for treatment. Following imaginal exposure, residual phobic avoidances were eliminated rapidly with *in-vivo* exposure. Where *in-vivo* exposure was tried first, it was either ineffective or only partially effective. Although the results of this series of case studies are uncontrolled they do indicate several possible directions for future clinical activity and PTSD research.

The order in which imaginal and *in-vivo* exposure was carried out may be an important consideration when planning treatment. In cases one and three, where *in-vivo* exposure was tried first, case one responded with reduced phobic anxiety but concurrent increase in other symptoms, whereas case three showed no response to treatment over eight months. Cases two, three and four showed improvements in dysphoria and depression following imaginal exposure and then rapid elimination of phobic anxiety when *in-vivo* exposure was carried out.

Possible explanations for these results can only be speculative at the moment. With anxiety disorders, such as phobias and obsessive–compulsive disorders, depression is known to inhibit the process of habituation to feared cues (e.g. Marks, 1987). Depression is commonly seen in PTSD patients and was a feature of all four cases. It may be that once the depression had lifted, *in-vivo* exposure was effective. However, this would not explain why *in-vivo* exposure was effective in case one, apparently to the detriment of other symptoms. Neither is it immediately apparent why imaginal exposure should result in improvements in mood.

Another possible explanation is that *in-vivo* exposure is unnecessary, imaginal exposure being effective for all symptoms. However, this is unlikely since cases two, three and four all showed marked phobic anxiety at the end of the imaginal phase of treatment.

The emotional processing model of fear reduction described by Foa & Kozak (1986) may account for some of our clinical findings. They suggest that techniques leading to emotional processing of fear, and therefore good clinical outcome, should include elements that activate the complete fear memory, including information on stimuli, the individual's response and the meaning of the fear. Treatment should also include information on behaviour that is incompatible with the person's usual response. During therapy, we should encourage patients to recall fear information that is as close as possible to their actual trauma. The better we do this, the more effective we will be activating the trauma memory and allowing processing to occur. Imaginal exposure to the actual trauma may be a more effective and controlled way of reviving patients' memories than *in-vivo* exposure.

Imaginal exposure may also give greater access to the 'meaning' elements of the memory. Foa *et al* (1989) argue that it is the personal meaning of patients' trauma experiences that is so important in understanding and treating PTSD. For example, case three may not have responded to *in-vivo* exposure to feared situations (such as the presence of males) because, although frightening, such situations did nothing to challenge her memory of her attack. Only by repeated exposure to the actual memory was symptom reduction achieved. The experience of a different response - in this case a calmer, non-fearful one - in the presence of the previously fearful memory helped emotional processing of the trauma.

However, *in-vivo* exposure may be necessary for activation and modification of other secondary fear memories, leading to full resolution of phobic symptoms. These symptoms may be acquired through a process of classic conditioning during the traumatic learning situations that produce most cases of PTSD.

The results suggest that when *in-vivo* exposure is ineffective with PTSD, imaginal exposure to trauma memories should be employed before abandoning behavioural approaches. Controlled research would now be indicated to assess the relative importance of *in-vivo* and imaginal exposure in PTSD so that the optimum combination of treatments can be determined.

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Pattern of Obsessive–Compulsive Disorder in Eastern Saudi Arabia

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In 32 Muslim Saudis with obsessive–compulsive disorder, compulsive acts (78%) and doubts (66%) were the commonest forms. Religious themes predominated in both the obsessions and compulsions.

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Obsessive–compulsive disorder (OCD) is one of the rarest conditions encountered in psychiatric practice (Ingram, 1961), although recent community-based epidemiological surveys show it to be more prevalent than hitherto thought (Meyers *et al*, 1984).

Lewis (1936) was "impressed by the frequency with which filth, harm, sex or religion give content to the obsessional ideas". Religious themes were evident in 50% of Jewish OCD subjects in Jerusalem (Greenberg, 1984) and were prominent in a series of OCD patients in Egypt – a Muslim country (Okasha, 1977).

From the age of 10 years a Muslim should pray five times a day, before which his/her body and clothes must be clean. Prayers consist of a set of sequential activities, preceded by 'body washings' ('*Al-Woodo*') – washing parts of the body a number of times in a fixed order. Urination, defecation or contamination by either nocturnal emission, sexual intercourse or passage of flatus, render the body unclean or 'impure' and necessitate washing it again.

OCD has not been reported before from Saudi Arabia, a conservative Muslim country. Accordingly, the authors carried out a preliminary study to investigate the pattern of OCD in a Saudi culture and to ascertain the impact of religion on the phenomenology.

Method

The study was conducted at the Psychiatric Out-patient Department of King Fahd Hospital of the University at Al-Khobar, Eastern Saudi Arabia. Nine clinics were held weekly, of which four were run by the authors. The hospital is a referral centre for a population of nearly one million. Patients were received from health facilities in the area and were randomly referred to the clinics by the appointment department. The study comprised consecutive Saudi subjects who attended the authors' clinics between January 1984 and December 1987 and who satisfied ICD-9 criteria for a diagnosis of OCD (World Health Organization, 1978). Those suffering from endogenous depression, schizophrenia or gross organic brain disease were not included. Subjects were evaluated independently by the authors using a semi-structured interview and standard mental-state examination. Data on age, age of onset of OCD, sex, marital status, family history and relevant stresses were recorded. Formal personality assessment was not performed for technical reasons.

The following operational definitions of OCD forms were adopted (Lewis, 1936):

(a) doubts: obsessional ideas of uncertainty, whether behaviour is performed or not
(b) thoughts: obsessional ideas other than doubts or obsessional questions with no ready answers
(c) impulses: obsessional urges to perform socially unacceptable acts
(d) fears: obsessional fears
(e) images: obsessional vivid mental impressions
(f) compulsions: obsessional motor acts.

Results

Thirty-two subjects (18 women, 14 men) fulfilled the designated criteria and all were Muslims. The mean (s.d.) age of the group was 26.6 (3.9) years and for the first onset of OCD was 20 (5.6) years. The onset was between 15 and 29 years in 84%, before the age of 15 years in 12% and above 29 years in 3%. The mean (s.d.) duration of OCD was 6.1 (4.8) years. The difference between men and women in age, age of onset or duration of OCD was statistically insignificant. Eight subjects were single, 22 married and two divorced. Family history revealed a similar illness in a first-degree relative of 11 patients (34%). Sixteen subjects reported unpleasant events during the year preceding the onset of their OCD. The most common of these were frightening events, reported by six patients, and included a scorpion attack, and fire and car accidents.

In descending order, the frequencies of OCD forms were: compulsions (78%) (these were invariably associated with another form), doubts (66%), thoughts (28%), impulses (22%), fears (22%) and images (3%). Table 1 illustrates the themes of the obsessions and the nature of the compulsive activities (rituals). The miscellaneous theme category involved door closure, work and safety of children. Compulsions included repetitions of prayers and/or their associated washings (*Al-Woodo*) and washings of the body or hands after visiting the toilet. The miscellaneous group of compulsions included smiling and unlocking bathrooms. Avoidance rituals were related to knives and heights. Compulsive looking at male genitalia was observed in a male subject.

OCD was associated with anxiety symptoms in 17 patients (53%) and depressive ones in another nine patients (28%).

Table 1
Obsessions and compulsions in 32 OCD patients

	n (%)
Themes of obsessions	
Religious	
prayers and/or body washings	16 (50)
body contamination	13 (41)
faith	11 (34)
Miscellaneous	6 (19)
Objects contamination	4 (12)
Death	4 (12)
Aggression	3 (9)
Sex	2 (6)
Illness	1 (3)
Nature of compulsive activities (rituals)	
Religious	
repeating	16 (50)
washing	12 (37)
Checking	10 (31)
Miscellaneous	4 (12)
Avoiding	3 (9)
Cleaning objects	3 (9)
Sexual	1 (3)

Discussion

In the majority of our subjects (97%) the onset of OCD was before the age of 30 years, and was preceded by stress in half of them, a finding which is similar to those of studies in other countries (e.g. Lo, 1967); however, the role of stress should be cautiously interpreted in the absence of a control group.

A review of the literature showed that between 5% and 10% of first-degree relatives of OCD probands manifest the same disorder (Marks, 1986). By contrast the percentage in our sample was relatively high (34%), yet a similarly high figure was reported in Egypt (Okasha, 1977).

Forms of morbid psychiatric phenomena need to be differentiated from their content (Jasper, 1963). Politt (1975) noted that compulsions and obsessions are the commonest forms of OCD; they are often associated with each other, and the occurrence of either alone is rare (Akhter, 1975; Marks, 1987). Likewise, in our study, compulsions (78%) and doubts (66%) were the commonest forms.

Cultural beliefs and concerns probably influence the content of obsessions and the nature of compulsions (Kiev, 1972). Saudi Muslim culture had an impact on the phenomenology of OCD in that the themes of obsessions were predominantly related to religious practices, namely prayers and/or their associated washings (50%). By contrast, religion was not a theme present in a British series of OCD patients (Stern & Cobb, 1978) and was infrequent (11%) among Hindu OCD patients; themes of dirt were common in the latter group and were attributed to the influence of Hindu scriptures which consider the body as basically dirty (Akhter, 1975). Moreover, the Saudi culture influenced the nature of commonly repeating compulsions (50%) in contrast with cleaning compulsions frequently reported in the West (Stern & Cobb, 1978; Marks, 1987). Prayer and/or their associated washings are the commonest shared daily activity among Muslims and dissatisfaction with their proper execution in some OCD subjects would easily give rise to doubts and repeating compulsions.

In our subjects compulsions with religious contents, being ego-dystonic, were not considered religious activities but morbid behaviour. Greenberg (1984) expressed similar views regarding rituals with religious colouring in some patients of his Jewish series with OCD.

Anxiety and depressive symptoms are frequent concomitants of OCD (Kringlen, 1965) and were also noted in this study.

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Polycythaemia Rubra Vera, Cerebral Ischaemia and Depression

DECLAN MURRAY and RICHARD HODGSON

A patient with polycythaemia rubra vera complicated by severe psychotic depression is described. There have been no previous reports of polycythaemia rubra vera associated with psychiatric morbidity.

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Polycythaemia rubra vera may lead to cerebrovascular occlusion, with effects ranging from transient ischaemic attacks to irreversible stroke and death (Silverstein *et al*, 1962). Because cerebral ischaemia can lead to affective disorder (Messner & Messner, 1988), psychiatric morbidity might be expected on occasion to result from polycythaemia rubra vera. Although loss of concentration and intellectual impairment occur, and improve on venesection (Willison *et al*, 1980), a MEDLINE computer search of the literature back to 1966 revealed no reports of psychiatric disorder associated with polycythaemia rubra vera. Standard textbooks of haematology state that "mental depression" (Wintrobe *et al*, 1981) and "depression and other psychiatric disturbances" (Firkin *et al*, 1989) do occur. We report a patient who, 10 years after polycythaemia rubra vera was diagnosed, suffered a severe depressive illness with psychotic features.

Case report

Mr G, aged 72, was married for 50 years, had no previous personal or first-degree family history of psychiatric disorder and had worked all his life, until he retired on medical grounds at the age of 58 owing to exacerbation of a chronic peptic ulcer. At the age of 61, he was diagnosed as having polycythaemia rubra vera and fulfilled the criteria of the Polycythaemia Vera Study Group (Berlin, 1975, 1976) having splenomegaly, a haemoglobin level of 22.2 g/dl, a red cell count of 9.76×10^{12}/l ($n<5.8\times10^{12}$/l), a red cell volume of 67.2 ml/kg ($n=18$–33), $pO_2=9.5$ kPa ($n=12$–15), a neutrophil alkaline phosphatase of 250 per 100 neutrophils, and later a platelet count of 665×10^9/l. He was managed on a regime of venesection, intermittent busulphan therapy, and 800 mg cimetidine and 100 mg allopurinol daily.

In September 1988 he was advised to have transurethral resection of prostate. In October 1988 he was admitted to a psychiatric ward, following six weeks of depressed mood, feelings of hopelessness, suicidal ideation, early morning wakening, and loss of interest, energy, appetite and weight (5 kg). During this period he had suffered frequent transient ischaemic attacks (TIA) with weakness of the left arm and leg lasting ten minutes before full recovery. He had no TIA for about one week before his emergency admission which was precipitated by a sudden, unprovoked attack on his wife. On examination he was depressed and suspicious, with paranoid delusions and auditory hallucinations. He was also disorientated in time. Two days later he had delusions of infestation and tried to stab himself with a coat hanger. The phenomenology was that of major depressive disorder with mood-incongruent psychotic features, and as reduced cerebral blood-flow was deemed to be causal, the diagnosis, according to DSM-III-R (American Psychiatric Association, 1987), was organic mood syndrome.

His disturbed behaviour was managed with intensive nursing care and haloperidol. Because his severe depression led him to refuse food, saying "the other patients deserve it more", maintaining adequate diet and fluid intake was not possible. Rapid remission was therefore essential and accordingly electroconvulsive therapy (ECT) was prescribed. After six treatments he made a good recovery and was discharged. He relapsed within three weeks into a retarded depression. He did not respond to lofepramine (210 mg daily) and after three months was readmitted and responded to a further course of eight ECT sessions and fluoxetine (20 mg daily). Fluoxetine was continued and at six-week follow-up he remained well, although he had residual anxiety symptoms.

Mini Mental State, a brief test of cognitive function (Folstein *et al*, 1975), was 26/30 (normal >25), and this remained borderline (23–26) throughout his management. Christenson's version of Luria's Neuropsychological Investigation (Christenson, 1979) showed impairment in abstract concepts and impaired retrieval of information from the more complex logical memory passage. These deficits had improved slightly on retesting six months later. Computerised tomography (CT) of the brain showed no focal lesion but generalised atrophy evidenced by widening of the sulci and of the intercerebral and Sylvian fissure, and periventricular lucencies around the frontal horns. Visually evoked flash and pattern-reversal responses were normal. Haemoglobin and other haematological parameters were normal, as was his blood pressure.

Discussion

This patient, with a sound pre-morbid personality and no personal or family history of psychiatric disorder, was apparently at low risk for the development of a primary depressive illness. He had evidence of organic brain insults (transient ischaemic attacks and cerebral atrophy on CT scan probably related to his polycythaemia rubra vera) which can lead to affective disorders (Starkstein & Robinson, 1989). Depression is common following stroke, the postulated mechanism being depletion of biogenic amines (Lipsey *et al*, 1984; Starkstein & Robinson, 1989). Such a mechanism may be invoked in this case, but the depletion of biogenic amines would be caused by a series of minor cerebrovascular episodes rather than a single major event. The finding that improved alertness followed venesection and correlated well with cerebral blood flow (Willison *et al*, 1980) may also be relevant to the development of psychiatric complications.

Depression may occur as a psychological reaction to organic illness (and in addition there was the stress of being advised to have a prostatectomy), but the acute onset of depression after a ten-year illness, and the lack of research evidence for a 'reactive' cause for post-stroke depression (Starkstein & Robinson, 1989) make the neurophysiological explanation more appropriate in our case.

The characteristic pathological processes of polycythaemia rubra vera, via cerebrovascular occlusion, could lead to psychiatric disorder. Systematic research could determine whether psychiatric morbidity is relatively common in this group of patients, and would help to resolve the apparent dissonance between the textbooks and the literature.

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Successful Treatment of Paraphilic Coercive Disorder (a Rapist) with Fluoxetine Hydrochloride

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A rape assailant with intrusive and persistent paraphilic rape fantasies was successfully treated with the antidepressant fluoxetine hydrochloride. Symptoms of impulsiveness, anxiety and depression were also markedly improved.

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Attempts to classify rape assailants into meaningful subcategories have emphasised either the sexual or aggressive aspects of the act. Recent studies suggest that a subgroup of rapists suffer with other paraphilias (Freund *et al*, 1983; Langevin *et al*, 1985; Abel *et al*, 1988). In addition, their rape fantasies and urges fulfil the current general diagnostic framework of paraphilias (DSM-III-R; American Psychiatric Association, 1987).

Abel and other revisionists of DSM-III proposed a subcategory of rapists, designated paraphilic coercive disorder. Criteria for the diagnosis required that over a period of at least six months, an individual had recurrent intense sexual urges and sexually arousing fantasies involving coercing or forcing a non-consenting person to engage in oral, anal, or vaginal intercourse. In addition, the person had acted on these urges or was markedly distressed by them. Whereas sexual sadists were erotically aroused by the use of force greater than necessary against the victim, the need for excessive force or the infliction of pain were not characteristic of paraphilic coercive disorder.

Despite the weight of the research evidence, this diagnostic category was excluded from DSM-III-R, not because the diagnosis was invalid, but because of legal and social concerns about the implications of labelling a subgroup of rape assailants with a discrete paraphilic diagnosis. In addition, there are no statistical data to indicate what proportion of rapists have paraphilic coercive disorder (Abel, 1989). The following case report demonstrates that perhaps this diagnostic subgroup might be treated successfully with our current psychopharmacological armamentarium.

Case report

Mr A was a 30-year-old single white male referred for evaluation after an abortive attempt to rape his mother. He had been discharged from an in-patient substance-abuse programme where he was treated for alcohol and marijuana abuse. He also presented with complaints of chronic anxiety and depression. At the time of referral he had been free of drugs and alcohol for one month. He was not subject to any criminal investigation before or during the course of the described psychiatric treatment.

Mr A had been in full-time employment and was living with his mother. The urge to rape his mother had been on his mind for several days. He attacked her, and they struggled for several minutes. Although the rape was unsuccessful, Mr A's mother suffered symptoms of post-traumatic stress disorder following the attack and required out-patient psychiatric treatment. The attack took place after Mr A was rejected by a peer female whom he wished to date. Despite being intoxicated with alcohol, Mr A did not suffer from a blackout during the attempted rape. Approximately two days after assaulting his mother, he went alone to the young woman's apartment while intoxicated, with a clear intent to rape her, knowing that he might need to murder her following the attack. He backed down from his plan while waiting in hiding, and soon afterwards admitted himself to the hospital for treatment of substance abuse. There was one prior incident of abortive sexual assault on his mother, four years before, but that was more an exhibitionistic exposure and did not involve physical struggle.

Mr A reported the onset of rape fantasies at the age of 18. In his fantasies, a woman was physically restrained, perhaps bound by the extremities and forced to be orally, anally, or vaginally penetrated. The fantasies did not include unnecessary pain, suffering or humiliation of the victim. Victims were always women that he knew. The deviant fantasies had become his primary means of achieving orgasm. In addition, Mr A had been "addicted to masturbation" since early adolescence and masturbated between one and four times per day, every day of his adult life. In addition to his rape fantasies and urges, Mr A had been peeping on his mother as his only other means of sexual stimulation. He thought of boring a hole in her bedroom or bathroom door but never did. His peeping took place several times per week.

Mr A's substance abuse began intermittently in early adolescence and progressed inexorably, with only brief periods of abstinence. By his 20s he used, at times, daily marijuana, and up to 225 ml of alcohol (spirits) per day. He had multiple blackouts, 'brownouts' (partial amnesias), problems with absenteeism at work, and had been stopped by police for driving while under the influence of alcohol. He had no arrest record. He reported that use of alcohol, cocaine, and amphetamines intensified his rape urges. Whereas rape fantasies started during adolescence, the progression to urges to act on the fantasies was not reported until his mid-20s when his polysubstance abuse was intensifying.

The patient described chronic anxiety since childhood. He had become socially avoidant and unable to speak in front of a group. He had a morbid fear that others might notice his hands shaking or that his handwriting would change when he was anxious. He did not complain of globus hystericus or inability to move his bowel or bladder in public lavatories. His social anxiety was particularly incapacitating when he met women of his own age. Thus, he was capable of sexual relationships only with relative strangers or prostitutes.

Mr A was an only child. He did not meet his biological father until his mother divorced his adoptive father, when A was in his early 20s. Both his adoptive and biological father were compulsive gamblers who suffered from alcoholism. Both were verbally abusive to A's mother, but A was not physically or sexually abused. In school, A performed poorly, had control struggles with authority figures, committed vandalism, played truant, lied to his teachers, and was expelled. He did not have learning disabilities. He frequently shoplifted until he was caught during adolescence. He described a period of depression with suicidal ideation while in secondary school, when he realised he did not 'fit in', was unable to form relationships with his peers, and began to have paraphilic coercive fantasies. This period preceded his more extensive use of drugs and alcohol. In retrospect, he described a chronic state of anxiety, irritability, low energy, impaired concentration and self-deprecatory ideation since childhood. During his teenage years he became a compulsive gambler and incurred significant debts. He was socially isolated except for a few drinking acquaintances. His major intimate relationship had been with his mother. He characterised his mother as an enabler who was overly involved in caring for him because of his multiple psychosocial problems.

There was a marked family history of psychiatric illness on the paternal side, characterised by alcoholism and pathological gambling; there was a maternal history of major depression requiring hospital admission.

Psychiatric assessment and treatment

Mr A met current criteria for major depression as measured by the Inventory to Diagnose Depression, a standardised self-report rating scale specifically designed to diagnose major depression according to DSM-III-R (Zimmerman & Coryell, 1988). His initial score on the 21-item Hamilton Rating Scale for Depression (Hamilton, 1960) was 21. He had no cleaning, checking or contamination rituals. He never had auditory or visual hallucinations or delusions. He reported no transient or consistent symptoms of mania or hypomania. His medical history was surprisingly normal and laboratory tests while in hospital were within normal limits.

Mr A met lifetime diagnoses that included conduct disorder, dysthymic disorder (early-onset subtype), superimposed periods of major depression without melancholia, social phobia, kleptomania, pathological gambling, and psychoactive substance dependence for alcohol and marijuana. His paraphilic diagnoses included voyeurism and paraphilic coercive disorder.

Mr A was seen weekly in supportive psychotherapy. At the beginning of treatment, he was no longer living with his mother. Since he had given up drugs and alcohol, he rated the intensity of his sexual urges as moderate and felt able to resist his most intense current urges. He attended Alcoholics Anonymous meetings sporadically. I chose to start him on fluoxetine hydrochloride because I had found it helpful in other paraphilic patients who were depressed and anxious. Fluoxetine was titrated initially at 10 mg per day (20 mg every other day). During the third week on medication, he stopped masturbating for several days in a row before relapsing. He reported concomitant lessening of both chronic and social anxiety. After three weeks, fluoxetine was increased to 20 mg per day. His symptoms began to show a diurnal variation (worse in the morning) that had not been apparent before medication. He spontaneously reported his voice was less monotonal. During week six, fluoxetine was raised to 40 mg per day. By week eight, Mr A reported 'normal', non-coercive sexual fantasies for the first time in his adult life. His rate of masturbation had gradually reduced to two or three times per week with both paraphilic coercive and normal heterosexual fantasies. One week later, he developed middle insomnia and anorgasmia, both reported side-effects of the antidepressant. The insomnia responded well to trazodone (100 mg at bedtime). The anorgasmia was treated successfully with cyproheptadiene (8 mg p.r.n.). Mr A reported a sense of calm and relaxation, exhibited social spontaneity, and a sense of humour. He denied any compulsion to masturbate and was satisfied by masturbating once or twice per week to non-paraphilic fantasies. During week 11 he reported the presence of "very mild" paraphilic fantasies and residual anxiety in the morning. Fluoxetine was raised to 60 mg per day, the current dose.

At the time of writing, Mr A had been free of paraphilia for seven months and had been taking fluoxetine for a total of ten months. He had begun to have women friends and expressed an interest in forming relationships. During the seventh month of out-patient treatment, Mr A suffered a relapse of gambling and severe alcohol abuse, requiring readmission to hospital. He reported remission of paraphilic urges, despite the relapse of the aforementioned addictions, until he ran out of his medication (for three weeks) before readmission. Restabilisation on the fluoxetine and trazodone combination brought relief of paraphilic symptoms again. Despite a hospital stay to combat his addictions, the patient suffered a second relapse of alcoholism and gambling and has dropped out of psychiatric treatment.

Discussion

This man fulfilled the criteria for paraphilic coercive disorder without sexual sadism. His rape fantasies began before the age of 20 and he met criteria for at least one other paraphilia. This is consistent with Abel's (1989) report on this paraphilic subgroup. Mr A's response to fluoxetine was gradual and appeared to be dose-dependent. The appearance of side-effects came at the same time as he reported the most dramatic improvement in his symptoms. Although the patient was in supportive psychotherapy and attention was drawn to his symptoms by the use of rating scales and direct inquiry, there was no other attempt to modify, coerce, extinguish or interpret his paraphilic symptoms.

An additional interesting aspect of the response to fluoxetine was the emergence of sexual fantasies of mutually consenting heterosexual intercourse as the paraphilic ones began to recede. These normal fantasies were reported as sexually gratifying. Mr A was greatly relieved not to need the rape fantasies for sexual satisfaction. He also reported great relief at not needing to masturbate daily.

It might be argued that this man's paraphilic activity might have remitted naturally, especially with sustained abstinence from alcohol and marijuana. His paraphilic urges were definitely intensified by the aforementioned substances, but he had reported the presence of fantasies and urges at other times when, previously, he tried to refrain from psychoactive drugs. His deviant fantasies started before his heaviest period of drug use. During the treatment, he suffered a relapse of alcoholism but remained free of paraphilic urges while he maintained himself on fluoxetine.

The current treatment of rapists includes incarceration, behaviour therapy (Abel *et al*, 1980; Pithers *et al*, 1988), group therapy, and biological treatment with libido-lowering anti-androgens (Lehne, 1988). There is a small case-report literature suggesting that thymoleptic agents may ameliorate paraphilias in the presence of depressive symptoms (Eyres, 1960; Ward, 1975; Snaith, 1981; Federoff, 1988; Cesnik & Coleman, 1989). Paraphilias have responded to imipramine, lithium, electroconvulsive therapy, and buspirone. This case report lends additional credibility that antidepressants may play a powerful role in the treatment of some paraphilias. It also suggests that male rapists who meet criteria for paraphilic coercive disorder should receive trials of thymoleptic medication.

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Spontaneous Improvement of Tardive Dystonia During Mania

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Two cases of bipolar affective disorder with tardive dystonic symptoms seemed to improve only with mood elevation, whether the latter occurred spontaneously or was 'induced' pharmacologically. Such cases could prove an interesting locus for the investigation of both affective disorders and tardive dyskinesias.

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Tardive dystonia is defined as persistent dystonic movements which emerge during or immediately after antipsychotic treatment. Burke *et al* (1982) listed the diagnostic criteria for tardive dystonia as follows:

(a) the presence of chronic dystonia
(b) a history of antipsychotic drug treatment before or during dystonia
(c) exclusion of known causes of secondary dystonia by appropriate clinical and laboratory assessment
(d) a negative family history of dystonia.

Being a persistent movement disorder that follows antipsychotic drug use, tardive dystonia was regarded as a type of tardive dyskinesia (e.g. Burke *et al*, 1982). Whereas classic tardive dyskinesia tends to occur in older patients, tardive dystonia appears to affect younger patients. The following assessments were suggested in an attempt to distinguish between the two types of dyskinesia (Marsden & Fahn, 1987; Burke, 1984): tardive dystonia (a) manifests itself clinically as dystonia rather than chorea, (b) affects younger patients, and (c) often benefits from anticholinergics.

It is, however, interesting that the prevalence of tardive dyskinesia in affective and schizoaffective disorders (26–83%) should be reported to be much higher than in schizophrenic disorders (18%) (Kane *et al*, 1985; Casey, 1984). The question of a special vulnerability to dyskinesia in affective disorders seems to be further supported by the data implicating the higher incidence rate of dyskinesia in affective disorders with short-term neuroleptic treatment and of a greater persistence after the termination of neuroleptic use (Kane *et al*, 1984).

Another issue for speculation is the 'mood-dependent dyskinesia' which implies a marked variation of dyskinetic symptoms in relation to mood alterations. Despite the fact that reports (e.g. Keshavan & Goswamy, 1983; Lal *et al*, 1988; Sachdev, 1989) of such cases are rare and limited to a few cases, the consistency in their results is worth noting. Casey (1984) summarised the important features of these cases, which are outlined below. (a) All the patients had manic–depressive disorder with sufficiently frequent episodes to be described as 'rapid cyclers' (except for one case of unipolar depression). (b) Tardive dyskinesia ameliorated or disappeared completely during mania. (c) Dyskinetic symptoms were generally aggravated during depressive episodes (except for one patient in whom dyskinesia subsided during the depressive episodes (Keshaven & Goswamy, 1983)). (d) Dyskinetic symptoms may or may not be present during the euthymic state. (e) Changes of dyskinetic symptoms sometimes occurred from a few days to a few weeks before the alteration of mood. The duration of neuroleptic use was relatively short, usually less than three years, and the patients were poor responders to the usual pharmacological approaches to manic–depressive illness.

Lal *et al* (1988) have reported a patient who had manic attacks on average every two years, except for one episode of depression, and who received neuroleptic prophylaxis for 12 years. Tardive dystonia improved markedly during the manic attacks as was observed in the above examples. We report two further such cases of dystonia.

Case reports

Case 1

Ms C, an unmarried elementary school teacher, aged 30, was referred to our clinic in 1985 with the diagnosis of manic excitation syndrome. It was reported that the patient had been displaying manic attacks lasting one to two months, which were preceded by a period of dysthymia every year since 1975. The case was diagnosed as manic disorder according to DSM-III (American Psychiatric Association, 1980) and Research Diagnostic Criteria. Previous attacks had also been without a psychotic dimension (no delusions and hallucinations present). There was no family history of affective disorders. A combined treatment of lithium and thioridazine (400 mg/day) was initiated. Neuroleptic treatment was gradually decreased over three weeks and discontinued while the lithium level was maintained at approximately 1 mEq/l. By the end of the fourth week, the patient almost resumed her pre-morbid mood and was discharged to be followed up, maintaining a serum lithium level of 0.8 mEq/l. Following her discharge from the clinic, torticollis was observed, appearing initially as a slight rotation of the neck to the left which aggravated in time to result in a dystonic posture persisting for four to five seconds.

Further questioning revealed that she had mild dystonia immediately before the manic attack which had resulted in her admission to our clinic. She had been prescribed a negligible amount of neuroleptics (haloperidol, 5 mg/day; thioridazine, 50 mg/day) and biperiden (2 mg/day) for prophylaxis from 1978 to 1982, after which neuroleptics were prescribed solely to treat attacks. Dystonia first emerged in 1984, while the patient was without medication and in a euthymic state, as a slight torsion of the head towards the left which was followed by persistent rotations. This symptom was overlooked by the patient and her family, and not expressed as a complaint, especially since it disappeared with the onset of the manic attack in 1985.

Consequently, with the reappearance of the dystonia (after becoming knowledgeable about its occurrence) lithium was discontinued and aetiological investigations to assess secondary dystonia (Fahn *et al*, 1987) were carried out without yielding evidence of a specific disorder. Having observed no change in the symptoms, lithium prophylaxis was reinstated after three months without drugs. The attacks recurred, however, with increasing frequency in the following years. We noticed that with each manic attack, dystonia disappeared completely or almost completely, only to recur in remission when the mood was restored to normal. Dystonia sometimes preceded the normalisation of mood by a few days. Despite hospital admission and maintenance of lithium at a level of 1–1.5 mEq/1, emergence of manic attacks necessitated the addition of thioridazine (100–300 mg/day). However, the attacks occurred more frequently, assuming a rapid-cycling character. It remains to be seen whether this was the natural course of the illness or a consequence of the pharmacological measures taken in an attempt to control dystonia.

Since 1986 attempts have been made to treat her dystonia (whose severity reached a considerable degree – dystonia in the neck, tendency to posturing, an internal rotation of the left arm starting from the shoulder, and pain in the left arm and wrist) by use of various drugs, with the following results. (a) Meclophenoxate (750–1250 mg/day for one month) had no significant effect. (b) Biperiden (6–18 mg/day for nine months) was initially used for one month in increasing doses when a manic attack appeared at 12 mg/day, thus resulting in a remission of the dystonia. Later, when it was prescribed again, this time with lithium for eight months in increasing doses, irritability was seen in the patient at a dosage of 18 mg/day, and there were no changes in the dystonia; it was decided to discontinue the drug. However, during this period, the patient took 12 mg per day of the drug secretly, without lithium, because she believed she had benefited from it. This medication was followed by another manic attack. It is possible that the manic attack had started before the patient took the biperiden secretly. Nonetheless, the dystonia remitted during this period. (c) L-dopa (100–200 mg/day) and benserazide (25–50 mg/day) combination was applied for two months after which a manic attack and remission recurred. (d) Clonazepam (2–6 mg/day for one month) was tried alone and in combination with lithium without success. (e) Lithium (0.8–1.0 mEq/l) and carbamazepine (400 mg/day) combination was applied for three months, during which dystonic symptoms were slightly ameliorated. This was followed by another manic attack and the disappearance of the dystonic symptoms.

At present, a combination of lithium and thioridazine is being used to try and control her mood and dystonia.

Case 2

Ms A, aged 33, a clerk in a bank, lived alone, and had a family history of a sister with both manic and depressive episodes. She was admitted to hospital in November 1984 having been diagnosed as suffering from a depressive syndrome (with a suicide attempt) and a paranoid component. Her history revealed a non-psychotic depressive attack in 1982, and a psychotic depressive attack which had followed a hypomanic phase in 1983. These episodes were treated with low doses of antidepressants combined with various neuroleptics for one to two months. After the attack in 1983, she complied poorly to the proposed neuroleptic prophylaxis (haloperidol 5–10 mg/day) in the eight months to follow. Three weeks after admission, a manic attack necessitated a change in the treatment which had consisted of a combination of amitriptyline (150 mg/day), haloperidol (10 mg/day) and biperiden (4 mg/day). Amitriptyline was replaced by lithium (serum level approximately 0.9 mEq/l) and the doses of haloperidol and biperiden were increased (20 mg/day and 6 mg/day, respectively). Her condition was normalised within one month and she was discharged from the hospital having been prescribed lithium only for prophylaxis.

She was admitted to hospital again in January 1986, with a manic attack, at which time we found out that she had discontinued lithium after three months. She was discharged one month later having responded to treatment with a combination of lithium and thioridazine (100–400 mg/day). Lithium prophylaxis was reinstated, although it could not be ensured that she complied sufficiently. However, during follow-up serum lithium levels were found to be maintained around 0.7 mEq/l. The manic attacks recurred with their previous frequency in 1987 and 1988. Attempts to raise her lithium level to 1 mEq/l were unsuccessful owing to her lack of co-operation. The attacks were generally managed in the same way as during her previous in-patient stay, that is, by a combination of lithium and thioridazine.

Dystonia reappeared one month after the remission of the manic attack in 1988 in euthymic phase as a rotation of the head to the right and was aggravated in a few weeks, becoming a tendency to posturing. No secondary causes of dystonia were found. Various treatment measures were taken because of the severity of the dystonia. (a) Biperiden (12 mg/day) in combination with lithium for one month did not result in a change in dystonia. Two weeks after the discontinuation of lithium, a manic attack emerged during which the dystonia remitted, to recur during the anxious-dysthymic period following the manic phase and to resume its former severity. (b) Lithium with carbamazepine (400–600 mg/day) could be used for one month only. (c) Tetrabenazine (100 mg/day for two months) did not have any effect on dystonia. (d) L-dopa (600 mg/day), benserazide (150 mg/day) and amitriptyline (75 mg/day) combination prescribed by another physician was followed by a manic attack a week after its initiation. The patient had to be admitted again as a consequence. During this period, the dystonia subsided. Once again, after a two-week combined therapy of lithium and thioridazine, as the condition normalised, the dystonia reappeared. Next, a combination of lithium (serum level 0.8 mEq/l), L-dopa (200 mg/day) and benserazide (50 mg/day) was started. The patient was discharged from the clinic in normal mood state, and her dystonia improved slightly. After her discharge, however, although she gave up her treatment and missed her follow-up, we were able to obtain information about the recurrence of attacks and the continuance of the same pattern of tardive dystonia. In our opinion, this case also has a tendency to become a rapid cycler.

Discussion

The two cases in our report, whose dystonic symptoms were followed for four years and one year respectively, complied with the assessments of tardive dystonia, as determined by Burke *et al* (1982).

Almost all of the common features of mood-dependent dyskinesias as summarised by Casey (1984) were shared by our cases: in both of the cases, dystonic symptoms disappeared completely or almost completely during the manic phase, and reappeared with the same intensity with the resumption of the euthymic state. The improvement in dystonia sometimes appeared to herald the alteration of mood a few days in advance. The consequence was the same whether the manic attack was spontaneous or 'pharmacologically induced'. Dystonia was characterised by resistance to treatment and subsidence with mood elevation. The attacks followed a bipolar but, contrary to other reports, an almost regular annual course, which could not be defined as rapid cycling. However, this characteristic pattern before the emergence of dystonia tended to change, to become rapid cycling. It does not seem plausible to explain this phenomenon solely by the pharmacological manipulations that could possibly have invited a manic attack. The case of mood-dependent dystonia described by Lal *et al* (1988) which, as far as we know, is the only one reported in the literature, shares some features with our patients: the attacks revealed a marked predominance of the manic pattern, and the pharmacological interventions to manage dystonia could sometimes induce a manic attack during which the dystonia ceased, to reappear with the same severity as the mood became normal again. In both Lal *et al*'s (1988) and our cases, non-responsiveness to lithium prophylaxis was a noteworthy feature.

The improvement of tardive dyskinesias and dystonias during the manic state has generally been interpreted as contrary to the established biochemical explanations of affective disorders and also as evidence stressing that these hypotheses are oversimplified (e.g. Casey, 1984; Lal *et al*, 1988). If mania is related to a monoaminergic overactivity, and depression is a monoaminergic hypoactivity, then tardive dyskinesia and dystonia, which emerge as a consequence of monoaminergic hypersensitivity, should be expected to subside during depression and exacerbate during mania. The situation, however, is exactly the opposite.

Despite evidence such as the resistance of the above cases to lithium prophylaxis, the predominance of manic attacks in the course of the illness, the tendency to assume a rapid-cycling character, and the emergence of dystonia one to two months after a manic attack, further research and evidence is needed before speculations are made. Nevertheless, cases of mood-dependent tardive dyskinesia/dystonia could provide a focus of research, containing important clues on both affective disorders and the emergence of tardive dyskinesias and dystonias.

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Is the Predisposition to Neuroleptic Malignant Syndrome Genetically Transmitted?

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A Japanese family consisting of a mother and her two daughters, all experienced NMS on therapeutic or subtherapeutic doses of neuroleptics. The mother and the elder daughter had past histories of severe neuroleptic-induced extrapyramidal symptoms. The predisposition to this syndrome may be genetically transmitted. We suggest that neuroleptic treatment should be introduced with extreme caution to a patient with a family history of NMS.

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Neuroleptic malignant syndrome (NMS) is a potentially fatal complication of neuroleptic treatment (Itoh *et al*, 1977; *Lancet*, 1984; Kellam, 1987). The prospective study by Keck *et al* (1987) shows it occurs in about 1% of patients treated with neuroleptics. This syndrome is characterised by catatonic symptoms (e.g. mutism, stupor), extrapyramidal symptoms (e.g. lead-pipe muscle rigidity, tremor), hyperpyrexia and autonomic disturbances (e.g. hypertension, tachycardia, profuse diaphoresis, dysuria). A recent review shows the NMS mortality rate to be 15% (Kellam, 1987), with the most common causes of death being respiratory failure, renal failure and cardiovascular collapse (*Lancet*, 1984). However, the exact pathogenesis and predisposing factors for NMS are not yet clear. In particular, there have been no reports of familial NMS nor suggestions that a genetic mechanism is involved in this syndrome. We describe a mother and her two daughters who all had NMS.

Case reports

Case 1

A 43-year-old mother presented suffering from catatonic-type schizophrenia (DSM–III–R; American Psychiatric Association, 1987). She was the third among four siblings, and had delivered two daughters at ages 22 and 24, then divorced at 37. She had several episodes of stupor with fever, but without muscle rigidity, between the ages of 22 and 30, when she was not on any drugs. Neuroleptic treatment was introduced in a hospital four months before presentation, for auditory hallucinations and delusions. However, neuroleptics had to be withheld for one month because of severe Parkinsonism, in spite of the co-administration of anti-Parkinsonian drugs. Treatment was resumed with haloperidol (4.5 mg), oxypertine (120 mg), trihexyphenidyl (12 mg) and amantadine (300 mg) daily. On day five, paralytic ileus developed and all medication was discontinued. On day eight, she was referred to our hospital.

The clinical symptoms and the laboratory findings upon admission are shown on Table 1. There was no evidence of infections, and a computerised tomography (CT) scan

Table 1
Clinical symptoms and laboratory findings of the present cases

	Case 1		Case 2	Case 3
	episode 1	episode 2		
Catatonic symptoms	Stupor	Stupor	Stupor	Stupor
Muscle rigidity	Lead-pipe	Lead-pipe	Lead-pipe	Lead-pipe
Tremor	+++	+++	+++	+++
Body temperature: °C	38.6	38.0	40.1	40.3
Autonomic disturbances[1]	+++	+++	+++	+++
CPK[2]: IU/l	911	1391	404	2303
Leucocyte counts: mm^3	4800	8500	13 900	13 500

1. Hypertension (>20 mmHg rise in diastolic pressure above baseline), tachycardia (>30 beats/min above baseline), profuse diaphoresis, urinary incontinence and dysuria.
2. Creatine phosphokinase level, normal value, 30–170 IU/l.

of her brain was normal. The diagnosis of NMS was given and conservative measures such as intravenous fluids, cooling and administration of an antipyretic were started. On days 11 and 13, she had grand mal seizures which were treated with diazepam (10 mg intravenously). On day 22, levodopa (50–200 mg/day, intravenously or orally) was started, since the catatonic symptoms and the muscle rigidity were still prominent. It took one week for the mutism and five weeks for the muscle rigidity to disappear by the levodopa treatment.

Eight months after the first episode had ended, she became talkative and aggressive to others and was given 5–10 mg/day of chlorpromazine, which induced trismus and opisthotonus. On day 24, confusion appeared and her intake of nutrients reduced. Her axillary temperature was 37.3 °C. Mutism, festinating gait and dysuria developed over the next four days. On day 29, the prescription was switched to bromperidol (1 mg/day). On day 33, bromperidol was withdrawn since a full-blown NMS was observed (Table 1). Ten days of dantrolene treatment (50–75 mg/day, orally), brought her serum creatine phosphokinase (CPK) level back to normal (35 IU/l) and the tremor disappeared. However, the fever resolved after ten days, as did the muscle rigidity and the mutism after two months from the introduction of levodopa treatment (50–200 mg/day, intravenously or orally). Thirteen months after the second episode had ended, she exhibited catatonic excitement with fever which was successfully treated with electroconvulsive therapy.

Case 2

The second case was her 22-year-old elder daughter who had residual-type schizophrenia. For three years she had been treated with several neuroleptics, some of them causing severe extrapyramidal symptoms in spite of the co-administration of anticholinergics. A brain CT examination was normal. She had been stable with levomepromazine (10 mg), lithium (600 mg; serum level: 0.37 mEq/l), biperiden (5 mg), diazepam (6 mg) and flunitrazepam (4 mg), daily. Suddenly, severe sleep disturbances appeared. She gradually became mute and her intake of nutrients reduced. On day four, tremor was observed and the axillary temperature was 37.4 °C. Screening tests for infections were all negative. On day seven, her clinical symptoms and the laboratory findings (Table 1) clearly indicated the development of NMS. All medication was discontinued and dantrolene treatment (40 mg/day, intravenously) was started. Ten days of dantrolene treatment brought her CPK level back to normal (51 IU/l) but her clinical improvement was unremarkable. In the next month, biperiden (10 mg/day) and diazepam (20 mg/day) were given intramuscularly with no effect. All the symptoms of NMS completely disappeared after three weeks of treatment with levodopa (50 mg/day, intravenously).

Case 3

The third case was the 20-year-old younger daughter who had catatonic-type schizophrenia. She had one episode of stupor with fever and autonomic disturbances, but without muscle rigidity or tremor, while not taking neuroleptics. She had been treated with several neuroleptics during the previous seven years. Her mental state had been stable with haloperidol (3 mg), zotepine (120 mg) and biperiden (6 mg), daily. One day, she became talkative and emotionally unstable, and her intake of nutrients reduced. Over the next 24 hours, fever (axillary temperature 38.2 °C), tremor, autonomic disturbances and mutism developed. The following drugs were given intramuscularly: on day two, levomepromazine (25 mg), on day three, haloperidol (5 mg) and levomepromazine (25 mg), and on days five and six, haloperidol (10 mg), while the oral prescription was changed to haloperidol (5 mg) and biperiden (3 mg), daily from day three. During this period, her body temperature continued to rise and she became stuporous. Extensive screening tests for infections showed no abnormal findings. On the night of day six, the development of NMS was unequivocal (Table 1). The serum level of haloperidol was 12.8 ng/ml. She died from respiratory failure and cardiovascular collapse the next evening despite an immediate discontinuation of the drugs and intensive supportive measures.

Discussion

The clinical symptoms of the present cases fulfilled the criteria for NMS proposed by Pope *et al* (1986). In case one, the causal relationship between the episodes and the neuroleptic treatments was clear. In the first episode, haloperidol and/or oxypertine was the causative drug. In the second episode, NMS began with chlorpromazine, and the full-blown syndrome was induced by bromperidol. In cases two and three, the causal relationships were not as clear as in case one since NMS often develops at the start of treatment, when the dosage is increased, or when a second drug is introduced (*Lancet*, 1984). The exacerbation in psychosis followed by physical exhaustion and reduced intake of nutrients, which are generally accepted as predisposing factors (Itoh *et al*, 1977), might increase the susceptibility to levomepromazine in case two, and to haloperidol and/or zotepine in case three.

All three patients were physically healthy. No other relatives of the present cases had suffered from psychiatric diseases or received neuroleptics. Case one had delivered cases two and three under general anaesthesia without any complications, although the details of the anaesthesia were not known. No other relatives, including cases two and three, had undergone major operations which had required general anaesthesia.

NMS is a rare complication of neuroleptic treatment (Keck *et al*, 1987). In all the present cases, the doses of neuroleptics were therapeutic or subtherapeutic, especially in cases one and two. All the cases had no physical diseases and the presence of organic brain disease was unlikely. These facts imply that the present cases had genetically determined susceptibility to NMS. In case three, the serum level of haloperidol was only slightly above the lower limit of the therapeutic window for haloperidol proposed by Santos *et al* (1989), suggesting that an extremely high neuroleptic level resulting from a pharmacokinetic variation such as poor metabolism was not involved in this case.

The cardinal symptoms of NMS, i.e. catatonic symptoms, extrapyramidal symptoms, hyperpyrexia, and autonomic disturbances, may be explained by excessive dopaminergic blockade in the basal ganglia and the hypothalamus (*Lancet*, 1984; Fricchione, 1985). In cases one and two, only partial or minimal responses were obtained by dantrolene, which is a directly acting muscle relaxant (Nelson & Flewellen, 1983), while the symptoms completely resolved after the introduction of the central dopamine agonist. In case three, the clinical status deteriorated as the dopaminergic blockade, especially that by haloperidol, proceeded. These facts all support the hypothesis that central hypodopaminergic states are the underlying pathophysiology in NMS. In case two, lithium might contribute to the development of NMS (Spring & Frankel, 1981), and it further supports this hypothesis since lithium inhibits the supersensitivity of dopamine receptors when they are exposed to a neuroleptic (Bunney & Garland, 1983).

Catatonia is a syndrome with multiple aetiologies, and neuroleptics are among the pharmacological agents capable of causing a catatonic state (Gelenberg, 1976; Fricchione, 1985). Thus, a common pathophysiology may be postulated between psychogenic catatonia and neuroleptic-induced catatonia (Fricchione, 1985). The latter may be a *forme fruste* of NMS, or may result in NMS as dopaminergic blockade proceeds (e.g. Fricchione, 1985). On the other hand, Cohen *et al* (1985) regarded NMS as an exaggerated form of neuroleptic-induced extrapyramidal symptoms. Therefore, a patient with a past history of catatonia and/or severe neuroleptic-induced extrapyramidal symptoms may be at high risk of NMS. The fact that cases one and three had catatonic states with fever while untreated with neuroleptics and that cases one and two had past histories of severe neuroleptic-induced extrapyramidal symptoms agree well with these hypotheses. Taking these findings all together, this family might have genetically determined vulnerability in the central dopaminergic systems, especially in the basal ganglia and the hypothalamus. Because of this predisposition, they might be liable to suffer from catatonia, severe neuroleptic-induced extrapyramidal symptoms and NMS.

The present report suggests that NMS has a genetic basis, although the information was not enough to specify the inheritance mode. In this context, the relationship between NMS and anaesthetic-related malignant hyperthermia, which is phenomenologically similar to NMS and has a genetic basis (Nelson & Flewellen, 1983), should be discussed. However, the study by Hermesh *et al* (1988) (and probably also case one in the present report) has shown no cross-sensitivity between these two disorders. Furthermore, as shown in the present report, in contrast to malignant hyperthermia which is of muscular origin (Nelson & Flewellen, 1983), the predisposition to NMS may be ascribed to the vulnerability in the central dopaminergic systems. The present report also suggests that a patient with a past history of catatonia and/or severe neuroleptic-induced extrapyramidal symptoms is at high risk of NMS. The latter hypothesis has been supported by Spring & Frankel (1981). We hope the present findings will be confirmed in further studies. From a clinical point of view, we suggest that neuroleptic treatment is introduced with extreme caution to a patient with a family history of NMS, since even small doses of neuroleptics may provoke NMS in such a predisposed patient as it did in the present cases.

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No Crossover Reactions to Citalopram or Paroxetine among Patients Hypersensitive to Zimeldine

BENGT-O. BENGTSSON, JÖNS LUNDMARK and JAN WÅLINDER

Five patients who reacted with the hypersensitive syndrome to zimeldine showed no reaction to one of two other selective 5-HT reuptake inhibitors, citalopram or paroxetine. This further strengthens the impression that the mechanism for the hypersensitivity syndrome induced by zimeldine does not seem to be related primarily to the 5-HT reuptake inhibition as such.

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Zimeldine (Zelmid, Normud), launched in March 1982, was the first antidepressant that selectively inhibited neuronal serotonin (5-HT) reuptake. In clinical studies it proved to be as effective as traditional antidepressant drugs (e.g. Huitfeldt & Montgomery, 1983) and also to cause fewer anticholinergic (Heel *et al*, 1982) and cardiovascular (Pottage & Groschinsky-Grind, 1983) side-effects.

However, zimeldine was withdrawn from common use in September 1983 because of a different type of adverse reaction. Some patients developed an acute flu-like syndrome comprising fever, signs of disturbed liver function and myalgia and/or arthralgia (Kristofferson & Nilsson, 1989). A few of these patients also developed peripheral neuropathy – in the most serious cases a Guillain-Barré syndrome (Fagius *et al*, 1985). The onset of the reaction usually occurred after 10 to 15 days, and in most of the cases the symptoms vanished promptly when treatment was stopped. The reaction was tentatively termed a hypersensitivity syndrome (HSS) and its frequency in clinical trials was reported to be approximately 1.5% (Nilsson, 1983). However, we found that 15 (47%) out of 32 patients aged over 65 years developed two or more symptoms in a HSS when treated with 50–200 mg of zimeldine daily (Bengtsson *et al*, unpublished). A high frequency of HSS has also been reported by Langlois *et al* (1985) (50%) and Warborg Larsen & Eggert Hansen (1984) (27%).

A genetic disposition and direct cellular toxicity, as well as pharmacological and immunological factors, have been considered in the aetiology of the zimeldine HSS (for a summary of the research see Kristofferson & Nilsson (1989) and Thomas (1989)). Positive lymphocyte-transformation tests in one of our studies (Kristofferson & Nilsson, 1989) and positive findings in the popliteal lymph-node assay (Thomas, 1989) both indicate an immunoreactive process.

Fears have also been raised that the HSS is not specific to zimeldine, but rather a reaction to the 5-HT reuptake inhibition in predisposed individuals. However, no HSS like that induced by zimeldine has to our knowledge been reported in the large series of patients hitherto treated with other selective 5-HT reuptake inhibitors. Furthermore, uneventful treatment with fluoxetine of three patients with hypersensitivity reactions to zimeldine has been reported (Chouinard & Jones, 1984; Montgomery *et al*, 1989). We report five patients who developed a HSS to zimeldine, but who were successfully treated with one or two other highly selective 5-HT reuptake inhibitors.

Case reports

The subjects were five elderly non-demented patients with recurrent major depressions who had all suffered from dose-limiting anticholinergic and/or cardiovascular side-effects on treatment with traditional antidepressants. Zimeldine and citalopram were both used on special licence and the treatment with paroxetine was approved by the regulatory authorities as part of a pharmacokinetic trial (Lundmark *et al*, 1989). During the initial treatment period all were in-patients at our psychogeriatric ward. Before treatment with any drug, physical and psychiatric examinations including biochemical tests were performed. During the treatment period weekly liver function tests including bilirubin, alkaline phosphatase (ALP), aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT), gamma-glutamyltransferase (gamma-GT) and lactate dehydrogenase (LD) were performed. During the first month of treatment body temperature was recorded daily. If adverse reactions appeared, clinical measures were taken to rule out causes not related to the drug.

Case 1

A 70-year-old woman with depressive illness was unable to tolerate tricyclic antidepressants owing to a disturbance of micturition. Pre-treatment examinations were all normal and she was given 100 mg zimeldine daily. On the 12th day of treatment she had a fever of 39.6 °C and complained about fatigue and muscular pain. ASAT and ALAT were both pathologically elevated. There were no clinical signs of infection and tests for bacteria in the urine and nasopharynx as well as a pulmonary X-ray were all negative. Treatment with zimeldine was withdrawn and she recovered from fever and pain within three days. The liver tests returned to normal after two weeks. She recovered from her depressive illness after electroconvulsive therapy (ECT) and was discharged from hospital. However, she relapsed after six weeks. She was then given 20 mg citalopram daily with good clinical effect. After six months of treatment with citalopram she was still without any signs of adverse reactions.

Case 2

A 77-year-old woman with a depressive disorder had suffered from severe orthostatism when treated with tricyclics. One year before the actual episode she had been treated for eight months with 100 mg zimeldine daily with good effect and without any adverse reactions. She relapsed in her depressive illness four months after stopping drug treatment and was readmitted to hospital. Pre-treatment tests were normal and she was again started on 100 mg zimeldine daily. On day 10 she developed signs of increasing arthralgia, had a temperature of 38.6 °C and abnormal liver tests. Plasma levels of zimeldine and norzimeldine were 110 and 750 nmol/l respectively (therapeutic range approximately 100–300 nmol/l for zimeldine and 400–1800 nmol/l for norzimeldine according to standards at the Laboratory for Neurochemistry at St Lars Hospital, Lund, Sweden). The zimeldine therapy was stopped the same day and three days thereafter liver function returned to normal and both fever and arthralgia abated. No other cause than zimeldine was found to explain the syndrome. The patient had ECT and long-term treatment with 20 mg citalopram daily was started. She recovered mentally and no sign of adverse reactions was seen during a five-month follow-up on citalopram.

Case 3

An 85-year-old depressed woman, who had previously experienced episodic confusional states when treated with low doses of tricyclic antidepressants, had a gastric cancer non-radically operated two years before the actual depressive episode. Pre-treatment tests were all normal and treatment with zimeldine (100 mg daily) was started. It had to be stopped on the 14th day because the patient developed severe muscular pain, a temperature of 38.2 °C and abnormal liver transaminase levels. Plasma concentrations of zimeldine and norzimeldine were 60 and 365 nmol/l respectively. Three days after treatment was stopped the body temperature was normal. The pain and the signs of disturbed liver function were gone within 14 days. She did not respond to ECT. During an antidepressive trial with citalopram (30 mg daily) no cross-reactivity to the zimeldine-induced adverse reaction was seen. The therapeutic response was poor and citalopram was withdrawn after nine weeks of treatment. Her physical status deteriorated and she died three months later because of spread of her malignant disease.

Case 4

A 67-year-old man was successfully treated with zimeldine (100 mg daily) for a depressive illness during four weeks at hospital. No side-effects were observed. Treatment continued after discharge, but on day 41 he was readmitted owing to an adverse reaction, with a temperature of 41.0 °C and arthralgia. The liver enzyme levels were elevated as was the blood sedimentation rate. A plasma protein electrophoresis showed signs of inflammation, but the tests for viral infection and a bacteriological test on the urine were negative. A pulmonary X-ray showed some minor basal atelectases but no infiltrates. The plasma level of zimeldine was 130 nmol/l and that of norzimeldine 150 nmol/l. Zimeldine was withdrawn and his symptoms disappeared completely.

Because of the rather late appearance of his adverse reaction (day 41) there were some doubts about its relation to zimeldine treatment. However, a new trial with zimeldine (100 mg daily) resulted in reappearance of fever and arthralgia after three days, making a zimeldine-induced syndrome highly plausible. One year later this patient was uneventfully treated with 30 mg paroxetine daily: after 10 weeks' treatment he showed no signs of a hypersensitivity syndrome.

Case 5

An 82-year-old depressed woman was treated for five weeks at hospital with paroxetine (30 mg daily). She had no fever or abnormal laboratory test results. Medication was stopped after four months, but she relapsed six weeks later and was started on 100 mg zimeldine daily. On day 12 she had a fever of 39.0 °C and had an increase in her gamma-GT value to an abnormal level. Treatment with zimeldine was stopped. One week after withdrawal her temperature returned to normal and the level of gamma-GT had begun to fall. After ruling out other possible causes her symptoms were diagnosed as mild reactions to zimeldine.

Discussion

The observed hypersensitivity reactions to zimeldine, from mild reversible flu-like symptoms to a high fever, pain, disturbed liver function and in a few cases a peripheral neuropathy, have been regarded as a possible threat to the use of all selective 5-HT reuptake inhibitors. The assumption has been that the mechanism for the adverse reaction involves the 5-HT reuptake inhibition. However, other selective 5-HT reuptake inhibitors now are in widespread use and still no hypersensitivity-like reaction has been reported. Our five patients with hypersensitivity reactions to zimeldine all tolerated treatment with either citalopram or paroxetine, both highly selective 5-HT neuronal reuptake inhibitors. They were closely monitored as in-patients during the initial three to four weeks' stay, and even mild side-effects would have been recognised. No such reactions were seen. Thus it seems that citalopram and paroxetine in this respect can be given safely to patients hypersensitive to zimeldine. Our findings also strengthen the hypothesis that the 5-HT reuptake mechanism as such is not involved in the hypersensitivity reaction to zimeldine. However, one must bear in mind that this conclusion is founded on a small number of patients.

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Dependence on Monoamine Oxidase Inhibitors in High Dose

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A 37-year-old woman with a personality disorder and chronic dysthymia developed a dependence on MAOIs. She ingested 440 mg tranylcypromine daily without any side-effects while taking no dietary precautions. The features of MAOI dependence and their resemblance to amphetamine dependence are discussed.

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Monoamine oxidase inhibitors (MAOIs) have been reported to possess some amphetamine-like stimulant qualities, in particular the non-hydrazine derivatives. Despite the wide use of these drugs in everyday clinical practice, there are few reports in the literature of tolerance to or abuse of MAOIs.

The most representative case reports of psychological and physical dependence on MAOIs are, to our knowledge, those of Shopsin & Kline (1976). The authors found the following common developmental and psychopathological features in their patients:

(a) a previous history of characterological sociopathic behaviour
(b) initial prescription of the MAOI because of 'depression'
(c) tolerance of the stimulant effect of the MAOI and progressive dose increase by the patient
(d) few or no side-effects, despite the large amounts ingested and the disregarding of any dietary rules.

All of these characteristics can also be demonstrated in the following case.

Case report

The female patient was born to alcoholic parents and grew up to witness their tempestuous relationship. Between 10 and 12 years of age she was repeatedly sexually abused by her father and tried to commit suicide at least twice. During late adolescence she ran away from home and married a 'depressive' boyfriend in order to 'start a new life'.

She first consulted a psychiatrist following an abortion at age 20, because of 'depression'. She complained of irritability, low energy, overeating, hypersomnia, poor concentration, excessive rumination and difficulty with making decisions. Over the next two years the mood disturbance remained unchanged, impairing her social functioning, despite psychotherapy and several trials with tricyclic antidepressants. After the birth of her first child she was admitted to a psychiatric hospital with psychomotor retardation, feelings of hopelessness and worthlessness, obsessive ruminations and suicidal ideation. She was treated with tranylcypromine (40 mg daily). After discharge she quickly attained her previous functioning level with only slight depression under continued medication. Nonetheless, she increased the MAOI dose progressively in the following months because of a return of 'fatigue' and loss of interest. Finally, she was ingesting a minimum dose of 80 mg tranylcypromine daily, which now resulted – in her own words – in "the happiest period of her life".

After her husband committed suicide she progressively increased the dose to 440 mg tranylcypromine daily and maintained this level over a two-year period without any serious side-effects, despite failure to adhere to any dietary precautions. She reported having tried to reduce the dose on several occasions ("to get rid of those pills"), without success, since each time her general state quickly deteriorated.

She reported herself longing for the 'energising' effect of the drug, for the feeling of 'freedom and power' it induced. Two and a half days after an attempt at an abrupt drug withdrawal she was admitted to an intensive care unit because of repeated generalised seizures followed by a status epilepticus. A blood and urinary analysis could not detect any other drugs.

In the following five years the patient was admitted to our clinic 11 times, mostly after marital disputes with her second husband or because of financial troubles. She complained of exacerbation of her chronic feelings of insufficiency, hopelessness and loss of interest. However, there was no diurnal variation, early morning awakening or loss of weight. She was overly dramatic, excessively emotional, irritable and given to attention-seeking behaviour. Information from close friends and previous hospital reports confirmed that this behaviour represented a long-term characterological trait. We repeatedly tried to discontinue her MAOI, but she always managed to gain access to this medication after discharge from hospital. Finally, at the age of 37, following severe financial troubles, she committed suicide with an unknown overdose of MAOI. According to her physician and her family she was not taking any other drugs at that time. On the insistence of her husband no autopsy was undertaken.

Discussion

Although MAOIs are universally prescribed as antidepressants, only a very small proportion of patients become dependent on them. These cases seem to have some common clinical features with respect to their personalities and their response to the pharmacological effects of the drug.

There is little doubt that there are factors in the subject's personality that predispose to drug dependence (Edwards *et al*, 1984). In the cases described by Shopsin & Kline (1986), the tendency to abuse MAOIs coincided with a previous history of abusing amphetamines as well as other drugs and/or alcohol. Furthermore, there were always sociopathic characterological traits, notably those sharing a common psychopathological and biological background with histrionic behaviour patterns, such as those observed in our case. It is, therefore, possible that patients with antisocial and/or histrionic traits are particularly vulnerable to developing drug-seeking behaviour after experiencing the euphoriant effect of the drug. One can find the description of amphetamine-like effects in reports of these patients, such as a feeling of 'speeding', 'euphoria' and the like, that provoked the unauthorised drug ingestion and the progressive dose build up.

There is some controversy as to whether the dependence-inducing pharmacological effect is related to all MAOIs or not. Although Shopsin & Kline (1986) support the view that all drugs of this category possess a stimulant-like 'energising' effect, it seems to be the non-hydrazine derivative tranylcypromine, with its side-chain configuration closely resembling the amphetamines, that is more often involved in cases developing a tolerance to and a dependence on MAOIs.

Another striking feature of the cases reported is the absence of serious side-effects despite the large amounts ingested and the patients' failure to abide by any dietary restrictions. Because of the fact that MAOIs, like amphetamines, increase the amount of norepinephrine, serotonin and dopamine available at the post-synaptic receptors, it is a noteworthy phenomenon that the high dosage over lengthy periods (in our case up to 440 mg daily), potentiated by the consumption of tyramine-containing foods, did not provoke any serious intoxication symptoms. Cloninger's (1986, 1987) suggestion that a low monoaminergic turnover might reflect the genotypal background of antisocial or histrionic personality traits (frequently observed among MAOIs abusers) could offer a plausible explanation for this extraordinary tolerance.

As with amphetamines, the abrupt discontinuation of MAOIs, especially of those with amphetamine-like properties, is reported to be followed by withdrawal symptoms (Pitt, 1974; Shopsin & Kline, 1976). This may also occur on stopping treatment with phenelzine, a hydrazine MAOI (Tyrer, 1984). Thus, in our case, a cardinal withdrawal symptom was the manifestation of generalised seizures followed by a status epilepticus two and a half days after the last drug ingestion.

In summary, MAOIs are used mainly in 'endogenous' or 'atypical' depression, when the hysteroid/dysphoric complaints are severe enough (Shopsin & Kline, 1976; Davidson & Pelton, 1986). In the latter case there is often an association with pre-morbid characterological disorders, as well as with polydrug and alcohol abuse (Akiskal, 1983). The potential for the development of tolerance to and dependence on MAOIs among these individuals demands a cautious approach as to the drug selected as well as close monitoring during treatment. In this context the common features of the rarely reported cases of MAOI dependence may offer a provisional guide of sorts for issuing a safe course of treatment.

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Contents: Catatonia and NMS/Dementia with parietal signs/Eating disorders in Asians/Selection of controls/Computerised tomography in schizophrenia/Tardive dyskinesia and HLA/Menopausal depression/EPDS by post/Educational status and neurological abnormalities in schizophrenia/Brain lesions and cognitive function in late-life psychosis.

Catatonia and NMS

SIR: In their paper "Catatonia: harbinger of the neuroleptic malignant syndrome" (*Journal*, March 1991, **158**, 419–421), White & Robins described five consecutive cases in which there was a prodromal period of withdrawal, followed by psychomotor agitation and excitement alternating with mutism. This was followed by stupor, fluctuating temperature, rigidity, autonomic instability, increased creatine phosphokinase (CPK) and white blood count (WBC), after administration of one to three doses of neuroleptics. The authors concluded that patients with catatonic excitement would be at risk for NMS.

The cases were interesting as their presentations were similar to lethal catatonia which was often described in pre-neuroleptic literature. In Mann's (1986) review of this condition, he noted similarities in these early descriptions. There was a prodrome followed by psychomotor hyperactivity, alternating with mannerisms, stereotypes, hallucinations, delusions and confusion, before lapsing into stupor with rigidity, hyperthermia, autonomic instability, and finally death. In the same paper, Mann also noted that in 31% of the cases he reviewed, the patients received neuroleptics before they lapsed into stupor and fever. The similarities between the two conditions extend to laboratory investigations such as increased CPK, WBC, erythrocyte sedimentation rate (ESR) and liver function tests (Fleischhacker *et al*, 1990).

Fleischhacker *et al* (1990) maintained that patients with psychomotor excitement are likely to receive neuroleptics and any subsequent fever and rigidity would be diagnosed as NMS; the reasons being the lack of awareness among clinicians of lethal catatonia and the emphasis on NMS in recent literature.

White & Robins reported that their patients received supportive treatment but failed to say whether they continued to be treated with neuroleptics or electroconvulsive therapy (ECT) for their psychosis. This is important because the treatment of lethal catatonia would be the continuation of neuroleptics and ECT (Mann *et al*, 1986).

The cases described by White & Robins could represent either NMS or lethal catatonia, and therefore we cannot agree with them that their five cases truly represented NMS nor that catatonic excitement would be a risk factor for NMS.

We do agree, however, that NMS is a life-threatening condition, and that neuroleptics should be used with caution. Patients with catatonic excitement could be treated with benzodiazepine so that any subsequent fever, stupor and rigidity could be more reliably diagnosed as lethal catatonia and so treated with neuroleptics and ECT.

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MANN, S. C., CAROSS, S. N., BLEIER, H. R., *et al* (1986) Lethal catatonia. *American Journal of Psychiatry*, **143**, 1374–1381.

AUTHORS' REPLY: Drs Tang & Ong cite Mann *et al* (1986) who, in their comprehensive literature analysis of lethal catatonia, described a similar course in many cases to that which we observed in our series: progression of the catatonic state into a rigid, febrile stupor after initiation of neuroleptic treatment. Furthermore, they noted a mortality rate of 78.4% for the catatonic patients who received only a neuroleptic.

Drs Tan & Ong remark that the clinical and laboratory features of lethal catatonia are indistinguishable from the NMS and yet they suggest that they need to be differentiated for management purposes. We have come to view these two conditions as having a common pathophysiology (probably on the basis of hypodopaminergic function) and not as separate entities. We see catatonia as a spectrum disorder with gradations from benign to malignant (and potentially lethal) variants. When neuroleptics are administered to catatonics there is a shift in the clinical state towards the malignant pole.

The term 'malignant catatonia' might more appropriately embrace all conditions presently labelled as 'lethal catatonia' and the 'NMS'. Aetiological probabilities would then need to be explored, e.g. psychogenic, drug-induced, viral, idiopathic. This concept may help to resolve the diagnostic dilemma raised by Drs Tan & Ong which is currently confounding work in this area.

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Sir: Craddock *et al* (*Journal*, January 1991, **158**, 130) are correct to point out that creatine phosphokinase (CPK) may be raised in many conditions other than NMS. It was for this reason that other possible causes of raised CPK were considered in the case we reported (*Journal*, September 1990, **157**, 437–438). We concluded that NMS, or a variant of it, was the only condition which could account for both the clinical picture and the elevated CPK, and suggested that carbamazepine may have prevented the development of a fever. Interestingly, Coulter & Corrigan (*Journal*, March 1991, **158**, 434–435) postulate a mechanism whereby this could have occurred.

Craddock *et al* describe a case of catatonia to illustrate that CPK is raised in motor disorders other than NMS. However, White & Robins (*Journal*, March 1991, **158**, 419–421) report five patients in whom catatonia immediately preceded NMS, and support the view that these conditions may have a common neurochemical basis. NMS was first described as a rare and frequently fatal condition, but further case reports suggest that this may be just one end of a spectrum of NMS. Stauders Acute Lethal Catatonia occupies an equivalent position in relation to catatonia, and the similarity is compelling. Kellam (1987) suggests that "the resemblance of these catatonic conditions to NMS is especially striking if the possibility is accepted that the extrapyramidal signs of NMS could be due to the neuroleptic drugs now almost universally involved".

The boundaries of catatonia and NMS are indistinct, and their independent status uncertain. Published reports to date have not identified features unique to either condition.

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Dementia with parietal signs

Sir: O'Carroll *et al* followed up demented patients with parietal signs (*Journal*, March 1991, **158**, 358–361). Their total dementia sample comprised 29 patients, of whom 18 were putative Alzheimer cases. It is clinically naive to assume that parietal disturbance caused by an infarct carries the same prognosis as parietal disturbance caused by other forms of cortical pathology. Therefore, their analysis, on their total sample, is irrelevant to the issue of heterogeneity within an Alzheimer's group. They do mention analyses on the 18 subjects whose Hachinski Index was less than or equal to four, but this group contained no patients under the age of 65 and no patients over the age of 86. In addition to this age restriction, the death rate of only six out of 18 over a four-year follow-up argues further that the group was unrepresentative of the population with global cortical dysfunction, which is the population in question. To omit the higher age-range patients is to omit just those patients with the lowest error score on a parietal test and the greatest longevity, and by so doing to minimise the chance of obtaining differential prognoses.

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Author's Reply: McDonald (1969) initially reported that patients with senile dementia who made 'parietal test' errors were (a) younger and (b) had a poorer prognosis in terms of life expectancy. In 1987, we failed to replicate (a) (*Journal*, January 1987, **150**, 114–117), and more recently we failed to replicate (b) (*Journal*, March 1991, **158**, 358–361). Dr McDonald is critical of our recent study. In reply:

We did not assume that parietal disturbance caused by an infarct carries the same prognosis as parietal disturbance caused by other forms of cortical pathology, rather we studied a mixed diagnostic group together with an Alzheimer sub-group as we wished to shed some light on the discrepant prognostic findings previously reported for parietal signs in mixed diagnostic groups (Whitehead, 1976; Whitehead & Hunt, 1982).

We did not omit patients on the basis of age. All psychogeriatric day hospital attenders who fulfilled our recruitment criteria at our initial sampling point were accepted. This left us with a sample whose ages ranged from 65 to 86 years.

Dr McDonald suggests that our sample was unrepresentative in view of the relatively low mortality figures (one-third of our Alzheimer sample died within a four-year period). Our sample was presumably early on in the course of the disease as they were day hospital attenders living at home. (Lishman (1987) states that death usually occurs within two to eight years of onset, with some cases living over 20 years.) Prognostic signs are surely more valuable early rather than late in the course of disease progression. Dr McDonald hypothesises that studying a sample with a higher age range would maximise the chance of obtaining differential prognoses on the basis of parietal test scores. This is a hypothesis which awaits independent empirical testing.

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Eating disorders in Asians

SIR: There is a growing trend among authors and researchers to 'blame' culture for any difference found between samples which originated in geographically different areas. The latest evidence of this is depicted in Mumford *et al*'s report on "Sociocultural correlates of eating disorders among Asian schoolgirls" (*Journal*, February 1991, **158**, 222–228). The authors surmised that the high prevalence of eating disorders among Asian girls is probably due to their "adopting Western patterns of reacting to personal conflicts and stressful life circumstances" despite noting high eating attitudes test (EAT) and body shape questionnaire (BSQ) scores to be associated with a more traditional cultural orientation and not with greater Westernisation.

Their comprehensive efforts and methods in carrying out this interesting study are indeed commendable, although a number of important aspects have not been taken into consideration. For example, social and economic class differences are known to influence eating attitudes (Eisler & Szmukler, 1985), and body shape preference (Ford *et al*, 1990); cross-cultural limitations of EAT 26 (Lee, *Journal*, January 1991, **158**, 131–132) and its reliability and validity are being questioned (Coker & Roger, 1990); and further still the cut-offs (and normative data) of EAT and BSQ for Asian populations are unknown. This last point has been acknowledged by the authors, but they have still opted to use similar cut-offs for subjects who have quite different life styles, eating habits, dietary content, norms and attitudes. Furthermore, the samples had significant morphological differences, which could confound eating attitudes; the relationship between eating attitudes and body weight has been reported to be complex (Chandrana *et al*, 1988). I think these flaws in method severely limit the interpretation of the data. There are other problems in using EAT in such a study (Lee, 1991). Replicating the factor structure in two populations may be evidence for cross-cultural conceptual equivalence and comprehension of questionnaire items, but that still overlooks and ignores attitudinal items specific to one culture in preference to another.

Later, the authors have suggested "internal conflicts and anxieties" and "intergenerational conflicts" – issues which can neither be easily confirmed nor discarded. The authors present fragile and untenable evidence in support of these explanations. Perhaps, the concomitant psychopathology should have been included as a useful variable. Individuals with distorted eating attitudes have been found to have additional psychological disturbances, such as low self-esteem, high concern for health, anxiety, depression and deviant behaviour (Chandrana *et al*, 1988). In Mumford *et al*'s study also, eating attitude differences could have resulted from psychological differences rather than cultural differences (or both).

Low prevalence of eating disorders in the Indian sub-continent may be a misleading inference. Conversations with psychiatrists would be of little help to Mumford and colleagues since eating disorders can hardly be considered to be a 'psychiatric' problem in this part of the world (where even frank psychosis and other mental disorders are perceived as psychological problems with a great reluctance!). Eating disorders perhaps land up in the medical, surgical and gynaecological clinics for the coexisting physical symptoms and complications, as was also pointed out by Lee (1991).

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FORD, K. A., DOLAN, B. M. & EVANS, C. (1990) Cultural factors in the eating disorders: a study of body shape preferences of Arab students. *Journal of Psychosomatic Research*, 34, 501–507.

AUTHOR'S REPLY: Dr Chaturvedi raises a number of points about our study, which boil down to two issues: (a) the robustness of our finding of a high prevalence of eating disorders among Asian schoolgirls in Bradford, and (b) the plausibility of our explanation and interpretation of these results.

The use of western questionnaires in non-western ethnic groups is certainly a risky business. It is incumbent on any researcher to demonstrate that this is justified in the population being studied. The Asian schoolgirls in Bradford were not of course a 'Third World' sample. Most had been born in Britain and all had been educated here, mixing daily in the classroom with indigenous English schoolgirls.

Lee (*Journal*, January 1991, **158,** 131–132) raised pertinent questions about the transcultural validity of the EAT. Our confidence in the EAT and BSQ as screening tests in this population is based firstly on the factor analyses, and secondly on the consistency between the results of questionnaires and of the semi-structured interviews. Our findings do not rest on the EAT and BSQ alone since we interviewed a broad sample of girls who scored highly on the questionnaires.

Socio-economic factors undoubtedly influence eating attitudes and EAT scores (Eisler & Szmukler, 1985), and represent a confounding variable in any cross-cultural study. We considered including measures of social class in our survey. However, social class is a culturally specific construct. There is no classification which is equally applicable to both Asian and indigenous British communities to allow valid comparisons to be made. Moreover, migrants frequently undergo an apparent fall in social status as a result of migration.

The second issue concerns the tentative explanation and interpretation which we offered for our results. To suppose that we are in the business of 'blaming culture' for any difference found between samples seems perverse. The notion of culture is an abstraction, for which there are many definitions. I favour Tyler's (1874) definition: "that complex whole which includes knowledge, belief, art, morals, law, custom, and any other capabilities and habits acquired by man as a member of society". Few would deny that there are significant differences between south Asia and Britain in these aspects of human social life.

It is certainly superficial to speak in such vague terms as 'cultural conflict'. It is important to specify hypotheses about the effect of cultural beliefs, attitudes and behaviour on the development of particular psychiatric disorders. Further carefully designed studies will be needed to test these hypotheses; these studies could usefully include measures of anxiety and depression, and disturbed behaviour.

Concerning the prevalence of eating disorders in the Indo–Pakistan subcontinent, there is a need for well-conducted epidemiological studies. We have surveyed three English-medium schools in the city of Lahore, using the same methods as in Bradford (Mumford *et al*, 1991). In a further study in rural Pakistan (Choudry & Mumford, 1991) we used our own Urdu version of the EAT; here factor analysis has highlighted problems in the conceptual validity of some EAT items, which we are currently attempting to address.

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Selection of controls

SIR: I read with interest the paper by Professor Morice (Cognitive inflexibility and pre-frontal dysfunction in schizophrenia and mania *Journal*, July 1990, **157**, 50–54). To enable assessment of the generalisability of these results to other schizophrenic and manic groups, it would be of interest to know how the subjects in each group were chosen (e.g. randomly? every *n*th patient presenting? on some representational basis? etc.).

I commend the attempt to select a "control group with a mean IQ lower than that usually obtained for control groups in psychiatric research", although this endeavour was unsuccessful in this instance! This is a problem that recurs throughout the literature pertaining to the Wisconsin Card Sorting Test in my opinion. Although a significant correlation between WCST results and IQ or educational level has not been reported, the trend seems always to be in the expected direction. That is, the putatively deficient group (viz. focal frontal, schizophrenic, etc.), in almost every case has a lower mean IQ or fewer years of education than the control group to which it is compared. Thus, for example, Heaton (1981) provides the following data: focal frontal only – IQ 95.5, focal non-frontal only – IQ 101.5, and normals – IQ 114.0; Weinberger *et al* (1986): schizophrenics – 12.5 years of education; controls – 16.8 years, and more recently, Miller *et al* (*Journal*, January 1991, **158**, 76–82) with late life psychosis (LLP) patients: LLP – IQ 84.5, controls – 109.5.

On the basis of these results, let us assume for the purpose of argument that overall IQ does impinge on WCST performance. Then looking at the results presented by Professor Morice, we find that for the schizophrenic patients, mean number of categories completed (3.1) is 1.6 standard deviations (s.d.) below the mean for the controls (5.2), a reasonable result considering that their mean IQ (84.5) is 1.4 s.d. below the mean for the controls (103.7). However, manic patients, whose mean number of categories completed (3.3) is similarly low (1.5 s.d. below the control mean) do not show such a discrepancy in their IQ results (mean IQ = 97.3, only 0.46 s.d. below the mean for the controls)! An interpretation of these results might be that, relative to their overall functioning level as measured by the full scale IQ, the manic patients show deficiencies on the WCST while the schizophrenic patients do not!

I would also make the observation that while 67% and 65% respectively of schizophrenic and manic patients showed these deficits, 33% and 35% respectively did not. It would be interesting to know the characteristics of these groups of patients (e.g. did the latter group of schizophrenics demonstrate increased incidence of auditory hallucinations, which might indicate a temporal rather than frontal focus etc.?).

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AUTHOR'S REPLY: Subjects were selected consecutively from the subgroups as described in the original paper. Although Mr Gale asserts that the attempts to select a control group with a mean IQ lower than that usually obtained for control groups were unsuccessful, his own examples belie this assertion:

Heaton	Miller *et al*	Morice
(1981)	(1991)	(1990)
114.0	109.5	103.7

Mr Gale is right to be intrigued by the relationship between general intelligence and performance on the Wisconsin Card Sorting Test. A dissociation did appear between the schizophrenic and manic/control groups. As he points out, the general consensus to date has been that while WCST performance can be impaired in the presence of average or above-average IQ, IQ *per se* does not affect WCST performance to any marked degree. This seems to be supported by results for the manic and control groups.

That schizophrenics demonstrated both low mean IQ and mean impaired WCST performance does not, of course, mean that low IQ only causes poor WCST performance, which Mr Gale offers as his alternative explanation. While theoretically this could be so, I can find no evidence in the literature to support it.

Rather, and to me a more persuasive explanation, the schizophrenic 'process' (whatever that may be) appears to result in a reduction both of measured IQ and of WCST performance. The manic 'process' appears, relatively at least, to spare IQ. These differences could possibly result from laterality differences in pre-frontal functioning in the two disorders.

Also, they could result from group differences in pre-morbid IQ. Unfortunately, a measure of pre-morbid IQ, such as the New Adult Reading Test (NART), was not used in this study.

There were no neuropsychological correlates of specific psychiatric symptoms in this study, and indeed this seems to be a common negative finding in schizophrenia research. While only 67% of schizophrenic subjects demonstrated impaired WCST performance, using cut-offs generated from this study, it is to be remembered that WCST performance is not the only measure of pre-frontal functioning. The pre-frontal cortex is a large area of the brain!

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Computerised tomography in schizophrenia

SIR: In the article entitled "Computerised tomography in schizophrenia, 15 years on" by Lewis (*Journal*, 1990, **157** (suppl. 9), 16–24) there is one statement that I feel is unnecessarily dogmatic and probably wrong. Lewis states that "the degree of ventricular enlargement is convincingly not a function of how long a patient has been ill". In a recent review of this issue (Miller, 1989) over 30 studies were considered which contained data on the statistical relationship between abnormalities of CT findings in schizophrenia and age, duration of illness, duration of hospital stay, or number of episodes. The majority of these studies found no relationship with duration of illness, but a few did show increased abnormalities in those patients who had been ill longer. The latter group of papers generally studied younger patients with shorter durations of illness.

Ventricular enlargement occurs to some extent with increasing age in normal persons, and this correlation might explain those cases where CT abnormalities in schizophrenia increase in magnitude with increasing duration of illness. However, in two studies, the appropriate statistical analyses were performed to show that duration of illness *does* have a correlation with degree of CT abnormality, independent of the age correlation.

More recent scanning studies have supported the suggestion that, at least in the first few years of a schizophrenic illness, there is a progressive increase in brain abnormalities. For instance, a one to four and a half year CT follow-up study by Woods *et al* (1990) showed progressive enlargement between the two scans. Of all follow-up scanning studies carried out to date, this study used the youngest, and probably the least chronic patients. DeLisi *et al* (1991) carried out a NMR study of very early-stage schizophrenic patients and found significant correlation between some measures of loss of brain substance and duration of illness. Thus, in contrast to the statement by Lewis, this issue is by no means settled.

In my own article, I suggested that there is progressive loss of brain substance during the manifest illness, which occurs mainly in the first few years of the illness, particularly when there are episodes of unchecked psychosis. This hypothesis could be of considerable significance, if correct. It may mean that, once a diagnosis has been made, very careful attention to antipsychotic medication to prevent, as far as possible, all further episodes of psychosis, can to some extent prevent progressive brain cell loss, and perhaps also the tendency towards progressive decline in mental function over the years of the illness.

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Tardive dyskinesia and HLA

SIR: I read with interest Brown & White's report (*Journal*, February 1991, **158**, 270–272) of their study on the possible association between tardive dyskinesia (TD) and the human leucocyte antigen (HLA), B44. However, I do not think that the methods and results reported either replicate or extend Canoso *et al*'s (1986) work, their stated aim, or support their conclusion that HLA B44 is not useful as a predictor of neuroleptic-induced TD.

Canoso *et al*'s 66 patients were all male, and no indication is given of their ethnic origin. Drs Brown & White included both male and female subjects, and although of a "similar ethnic origin", their exact ethnicity is not stated. It is very unlikely that 40 long-term patients of a Scottish psychiatric hospital could be reasonably compared with 66 patients at a Massachusetts Veterans Administration facility for something as ethnically dependent as HLA haplotype.

Unlike the Scottish sample, Canoso's patients did not all suffer from schizophrenia; 19 of the 66 had other diagnoses. Furthermore, Canoso used Research Diagnostic Criteria and not DSM–III (American Psychiatric Association, 1980) for diagnosis. The difficulty in comparing the two studies is further compounded by Canoso assessing only orofacial movements, and using a score of 14 on the Rockland scale to separate moderate/severe, from mild, TD; the Scottish group used the same scale without qualification of the score accepted as indicating the presence of TD, and included an assessment of all body areas. The use of an arbitrarily high or low score would inadvertently consign TD patients to the non-TD group, or vice versa, respectively, and thus cancel out any real differences in haplotype between the two.

Hence, on the basis of differences in ethnicity and gender, and the use of various diagnostic criteria for both psychiatric illness and TD, comparisons between the Scottish and American results are, at best, difficult.

Turning to the conclusions of Drs Brown & White; the sample is clearly not large enough to confirm or refute an association between HLA B44 and TD, such is the degree of polymorphism at the HLA locus. Again, the comparison of their group with 500 British subjects tissue-typed for other reasons, is not tenable, as no indication is given of the sex, age or ethnicity of the latter.

It is interesting to note that one other study (Metzer *et al*, 1990) failed to replicate Canoso's findings in 58 patients at an Arkansas Veterans Administration facility, but did find that possession of the DR4 antigen increased the relative risk for TD to 3.04, and that all patients with the extended haplotype B44–DR4 had neuroleptic-induced movement disorder. Drs Brown & White's suggestion of an association between schizophrenia and B44, although not supported by research to date, perhaps indicates that the extended B44–DR4 haplotype predisposes to both schizophrenia and TD, or that the latter is yet another symptom of the former as some authors suggest (Crow *et al*, 1983). The A1–B37 extended haplotype has already been implicated in increasing the relative risk for schizophrenia to 15.87 (Metzer *et al*, 1988).

Clearly, further research is needed to determine the evasive links that exist between schizophrenia, TD and HLA haplotype.

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Menopausal depression

SIR: Much of Dr Wheatley's letter (*Journal*, March 1991, **158**, 431–432) on menopausal depression is a criticism of the study by Montgomery *et al* (1987) in which I carried out the psychiatric assessments, and there are several misunderstandings in what he says.

His main concern is that the instrument used to detect emotional symptoms was not specific to depression and did not enquire about 'biological' and some other symptoms. This was because our interest was not confined to depression. We preferred to assess all neurotic symptoms because this patient group, like many other out-patient populations, does not fall conveniently into one diagnostic category. Menopausal women experience a mixture of neurotic and physical symptoms, but few biological features of depression, hence the use of the SRD–30 (Kellner & Sheffield, 1973), which had sub-scales for anxiety, depression and somatic complaints and which has frequently been used in studies of a similar kind. Despite this, Dr Wheatley believes that psychopharmacologists have not heard of the SRD–30. They may however, have heard of the Clinical Interview Schedule (Goldberg *et al*, 1970) which we used to validate the SRD–30 scores.

His letter also manages to miss out our main finding: that psychological disorders responded to HRT in peri-menopausal but not post-menopausal women. The implication is that a hormonally sensitive sub-group may exist – although this is not to say that HRT is the treatment they need – but post-menopausal women who are depressed should be treated like anyone else, i.e. pharmacologically and, equally important, psychologically.

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This correspondence is now closed. I.P.

EPDS by post

Sir: The Edinburgh Postnatal Depression Scale (EPDS; Cox *et al*, 1987) is a 10-item self report scale developed as a screening tool for use by health visitors with a post-partum population. It is short, simple, and easy to score and administer. For these reasons it has become very popular as a research tool, although this was not its original purpose.

We are currently using it as part of a study of womens' experiences of screening during routine antenatal care. Our earlier work (Green, 1990) and that of others (e.g. Watson *et al*, 1984) had suggested that low post-natal emotional well-being might be predicted from low antenatal mood. We therefore chose to administer the EPDS at 35 weeks of pregnancy and at six weeks post-partum. We have complete data from over 1300 women.

The EPDS has been validated for antenatal use by Murray & Cox (submitted), who observe that "Fortunately, the EPDS contains no specific reference to the post-natal period so none of the items had to be altered for this study". While this is true, we would like to draw attention to one of its items which, it is clear from our own data, is capable of a different interpretation when asked antenatally. The item in question is (within the past week) "The thought of harming myself has occurred to me". This item is intended to detect suicidal thoughts, but, to a woman well advanced in pregnancy, clumsy and ill-balanced, it can be read as "I am preoccupied by the possibility of falling and hurting myself" or even as concern that harm might befall her during labour and delivery. Accordingly, we have found some women scoring the maximum on this item while having relatively low scores overall, and some have added explicit comments which confirm that their interpretation was not that originally intended. We would therefore warn others who may be using the EPDS in late pregnancy to treat this with caution.

We have yet to complete our analysis, but our impression is that, even without the complication of the last item, many women have been obtaining very high scores at 35 weeks. This was also observed by Murray & Cox and is consistent with the findings of Watson *et al* (1984).

Our use of the EPDS has been in postal questionnaires as part of a longitudinal study. Women therefore complete the scale in their own homes at a time of their own choosing. By 35 weeks they are used to answering questions about their feelings and in many cases a relationship has been developed, as one woman said "It's like having a penfriend". Any of these factors may account for the fact that we are obtaining some very high scores and a mean level post-natally that appears to be higher than is usually reported. We have observed a tendency for scores on the Spielberger State Trait Anxiety Inventory (STAI) to be lower when sent through the post. We would therefore be interested to hear from others who have sent the EPDS through the post, or who have any other data on postal assessment of emotional state.

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Educational status and neurological abnormalities in schizophrenia

Sir: An interesting finding reported by Rossi *et al* (*Journal*, November 1990, **157**, 735–740) is the significant correlation between educational status and neurological impairment among schizophrenic patients. However, the authors have not elaborated on the nature of this association and have not discussed the implications of this important observation. In a comparable study of neurological soft signs (NSS) in schizophrenic patients and their first-degree relatives (Shaji *et al*, 1990) we found less-educated subjects having more NSS even after controlling for the effects of age and sex. The possibility of an early-onset illness leading to poor educational attainment as an explanation for the association seems unlikely as there was no significant excess of NSS in the subgroup of patients with an early onset of illness. Another possible interpretation would be that NSS may be the evidence of an early cerebral insult and the resultant central nervous system dysfunction may lead to poor educational attainment even before the onset of illness. The brain dysfunction may also act as a predisposing factor, at least in a subset of patients, and may be responsible for the clinical expression of schizophrenic syndrome later on. Although these hypotheses sound attractive there does not seem to be enough evidence as yet to provide definitive answers.

Magnetic resonance brain imaging (DeMyer *et al*, 1988) of schizophrenic and normal subjects have shown that brain size is positively correlated with education. Lewis (1990) after reviewing a number of CT scan studies concluded that a range of demographic factors including educational level were important in determining various structural brain parameters. Such studies highlight the importance of controlling for the effect of education in studies of human subjects where brain size is the dependent variable. Although there are no definitive studies to correlate NSS and brain pathology using the newer techniques of imaging, this area needs to be pursued. If indeed there is a correlation, assessment of NSS could be considered as an inexpensive, simple method of studying neurological impairment. Issues raised by Rossi *et al* regarding the methods of assessment of NSS need careful consideration.

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Brain lesions and cognitive function in late-life psychosis

SIR: Miller *et al* (*Journal*, January 1991, **158**, 76–82) published the results of their study of 24 patients with late-life psychosis. Patients had significantly more brain abnormalities on magnetic resonance imaging (MRI) scan than controls. In particular, despite normal neurological examinations in all but two of the patients, 25% of this group had cortical or white matter infarctions on MRI, compared with 7% of controls. Although the patient group had more abnormalities on neuropsychological testing, their mean Mini Mental State Exam (MMSE) score was 28/30 and none met clinical criteria for dementia.

These findings are very similar to our own (Flint *et al*, 1991). We studied 33 elderly patients with normal neurological history and examination, and a mean MMSE score of 27/30, meeting DSM–III–R criteria (American Psychiatric Association, 1987) for delusional disorder, schizophrenic disorder (late-onset type), and schizophreniform disorder. Of the patients undergoing CT brain scan, 31% were found to have cerebral infarction, mostly affecting the frontal-subcortical system. In addition, the presence of infarction was inversely correlated with social risk factors (failure to marry, social isolation) previously described for 'late paraphrenia', suggesting that stroke, by itself, is a potent mechanism in the pathogenesis of late-life psychosis.

Although Miller *et al* did not specifically examine treatment response, their impression was that many of their patients were treatment resistant. They speculated that the underlying brain disease contributed to a poor prognosis. In our study, subjects with brain infarction were indeed significantly less likely to respond to treatment. Because of the appearance of disabling side-effects, patients with CT evidence of stroke could only tolerate, on average, half the dose of antipsychotic medication compared to those without infarction. Had this 'organic delusional' group been able to tolerate higher doses of medication they may well have shown more symptomatic improvement. Interestingly, several studies, including Holden's (1987) all found significantly worse outcome in late-onset paranoid patients with cerebral organicity.

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A HUNDRED YEARS AGO

Our Library Table

Oeuvres Complètes de J. M. Charcot. Tome IX. Paris: Aux Bureaux du *Progrès Medical.* Lecrosnier et Babé. 1890. – This, the ninth volume of Professor Charcot's writings, which are being so faithfully collected under the careful editorship of his former pupil, M. Bourneville, contains some of his earliest as well as his most recent contributions to neurology. For side by side with the memoir upon cerebral haemorrhage, written in conjunction with M. Ch. Bouchard, in which the invariable presence and the etiological importance of miliary aneurysm in such cases were first pointed out, we find papers upon hypnotism and hysteria, to which Professor Charcot has devoted so much thought and attention of late years. The volume, too, contains a reproduction of his observations upon metalloscopy and metallotherapy made in 1877. We are not quite so much inclined as is the able editor to regard these curious records as of the first importance, and it is certainly remarkable how transient was the interest – keen enough at the time – taken in the subject. However, as a matter of history, and as exemplifying the manner in which Professor Charcot investigated this by-path of neurology, the republication of these papers is welcome. Hypnotism is treated at considerable length, and we are glad to find in an appendix the excellent paper of Babinski, which sets forth clearly the views of the Paris school on this subject, as opposed to that of Nancy. The reader should peruse M. Babinski's essay first, before committing himself to the study of the experiments detailed in M. Charcot's memoir. The place of static electricity in therapeutics, and its application especially to the treatment of hysteria, form the final part of the volume.

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Researched by Henry Rollin, Emeritus Consultant Psychiatrist, Horton Hospital, Surrey.

British Journal of Psychiatry (1991), **158**, 868–870

Books Reconsidered

One Flesh: Separate Persons: Robin Skynner

There are probably few practitioners of marital and family psychotherapy who are not aware of the work of Dr Robin Skynner. In his own unique style, he has been part of the vanguard of the development of thinking and practice in these fields. Together with colleagues, he was instrumental in setting up the Group Analytic Practice, the Institute of Group Analysis and the Institute of Family Therapy. He is a teacher, and a prolific writer, and many of his papers, articles and lectures have recently been collected and published in two books (Skynner, 1987, 1989).

Dr Skynner is also widely known to a lay audience, largely through his excellent book co-written with actor and author John Cleese (Skynner & Cleese, 1983). In this book in particular, Skynner demonstrates his capacity to translate complex theoretical and clinical concepts into ideas accessible to a general reader. The sequel to this book, currently being co-written, is keenly awaited.

Much of what Skynner is known for, and what underlies much of his work, was set down in *One Flesh: Separate Persons* in 1976. As the sub-title indicates, this book outlines his "Principles of Family and Marital Psychotherapy". In the opening sentences of the book, Skynner puts marital and family psychotherapy into context. He writes:

> "The institution of the family stands in a peculiarly central, crucial position. It faces inward to the individual, outward toward society, preparing each member to take his place in the wider social group.... Our needs for physical, emotional and intellectual exchange, and for nurturance, control, communication and genital sexuality, can all exist side by side and find satisfaction in harmonious relationship to one another.... It [the family] has enormous creative potential... and it is not surprising that, when it becomes disordered, it possesses an equal potential for terrible destruction."

It is exactly because marital and family life is so central to public and personal mental health, either in promoting it, stunting it, or, at worst, damaging it, that it is rightly the concern of the mental health profession. Marital psychotherapy and family psychotherapy should therefore stand alongside individual and group therapies as potential treatments of choice.

In his introduction to the book, Skynner writes of this text being an attempt to provide a review of the various theories of marital and family psychotherapy, with practical guidance and clinical illustrations which may enable professionals to apply the ideas to their own practice. At the time of writing, no such introductory general text was available. What did exist tended to concern itself with either family psychotherapy or marital and sexual therapy, and took either a psychoanalytic orientation or a systemic one.

What is of particular interest and value in this book is the attempt Skynner makes to relate and integrate family, marital and sex therapy viewed from a range of theoretical and conceptual positions. He refers to this himself when, in his chapter on "Developmental Sequences" (Chapter 2), he writes:

> "A generally useful classification (of the sequences of events in childhood development) is based on a combination of Freudian and Kleinian developmental concepts, modified in the light of elaborations by other individual-centred therapists such as H. S. Sullivan and E. Erikson, and also by researchers in group dynamics and development, including, Bion, Bennis, Schutz and Durkin."

He goes on to acknowledge that followers of any one of these schools may justifiably feel that some violence has been done to their conceptual schemes. He specifies, for example, that there may well be real differences between Klein's 'positions' of emotional development and Freud's 'stages'. However, he justifies his integrative approach by saying that he is attempting to find the common patterns which must underpin all these various theories.

This lack of theoretical purity, this eclecticism, is one aspect of the book which some readers may find difficult, particularly when many of the clinical illustrations which pepper the book tend towards the anecdotal and personal and so do not readily avail themselves of critical theoretical and clinical examination. However, this criticism, although probably valid, misses Skynner's purpose in writing the book, and also the value that the book still has today. Skynner wanted to introduce the relative beginner, be he/she a psychiatrist, social worker, counsellor or psychologist, to an overview of the variety of approaches to thinking about and working clinically with couples and families. He was clear in the book that an integrated, eclectic approach is the one he finds most useful for his clinical work. The value of the book goes beyond that: it allows the practitioner to discover, from his own experiences, which of the conceptual and technical models he finds most therapeutically valuable. It is this that I personally found most satisfying when I first read the book on its publication, and still do now on re-reading it. It has always remained a textbook to dip into.

The book is written in two parts, theory and practice. Or, as Skynner writes, concepts and applications.

In the first part, he systematically goes through general systems theory, a developmental scheme (eclectic, as outlined above, but heavily influenced by ego psychology), psychoanalytical theories, modelling and social learning theories. Throughout, there is a constant attempt to show the overlap and similarities between these different models. Three of the nine chapters in this first part concentrate on the marital relationship. This, I believe, is appropriate as the couple are at the heart of the family. Children internalise not just models of their parents in isolation but also, probably more importantly, of their parents in relation to each other and in relation to them. These internalised images then become part of the blueprint which, largely unconsciously, is taken not only into their own marriages and families, but into all their social interactions and relationships.

Skynner gives a very clear and concise outline of the psychoanalytic object-relations model of marital interaction, and specifies the developmental and defensive aspects of unconscious partner choice. He also discusses with conviction the view that in the case of most children and adolescents who are referred for psychotherapeutic help, the level of the child's developmental arrest, or the nature of the symptom being presented, relates very closely to pathology in the parental relationship. Whether understood in systemic terms or in terms of psychoanalytic notions of projection and projective identification, the child may be said to become the victim of the emotional conflicts of the parental couple.

In the final chapter in this first part, Skynner addresses 'The Ethics of Change'. He asks such questions as what right we (as practitioners) have to attempt to change others; what the motivations of referrers may be; whether change is possible; and, if so, whether it is desirable. It is a thought-provoking chapter and addresses issues which are often taken for granted or overlooked.

In the second part of the book, the author turns to clinical practice. He outlines different therapeutic models and distinguishes between them. He then describes his own clinical practice, across the range of his clinical work including that of couples groups which he often co-ran with his wife. Throughout, there are many clinical examples and vignettes to illustrate what is being discussed.

I was particularly interested to read his views on transference. He writes that he does not encourage the transference by drawing it onto himself, and only interprets it if it is getting in the way. He also says that the wide spacing of the interviews, and his more natural, active, and spontaneous behaviour diminish the development of transference phenomena. Finally, he says that as the therapist he offers himself explicitly as an expert and this, too, limits the development of the transference.

How much these factors actually do limit the development of the transference is open to debate, and Skynner seems to imply this when he goes on to say that, despite all his best efforts, marked transferences to the therapist do develop, He sees this as usually being concerned with defensive needs, either in the family or in the therapist. This view is in sharp contrast to a purer psychoanalytic understanding which would view transference as inevitable and unavoidable, and would value the transference feelings and enactments evoked by the psychotherapeutic encounter as being a rich source of information about the family members and their images and expectations of relationships. This view is not one simply held by individual psychoanalytic psychotherapists, but one that family and marital psychotherapists would hold (e.g. Box *et al*, 1981; Scharff, 1982). However, this may be an unfair observation since the application and adaptation of psychoanalytic theory and practice to marital and family work has gone on since the publication of Skynner's book. I suspect, however, that he would still hold to his original view.

The next five chapters discuss a variety of technical issues such as indications and contra-indications for marital and family work; the use of multi-family and couples groups; and training and teamwork. This second section finishes with a chapter outlining the family therapy with a particular family carried out over 16 sessions at three or four weekly intervals by Dr Skynner and a female co-therapist.

Without doubt, exactly as intended, this book remains an excellent introduction to marital and family psychotherapy. In its 400-plus pages it is informative, provocative, practical and always lucid and accessible. Although an introductory text, it is ambitious in its aims and raises many issues for debate and discussion. Like a good therapist or teacher, Skynner makes the reader pause and think for himself, and come to his own conclusions.

I would like to raise two further thoughts. The first is a criticism, the second is a point of interest.

To take the criticism: there are points in the book when Skynner could be accused of sexism and chauvinism. Sometimes his descriptions of the wives and mothers in the families he is writing about are rather clumsy. It seems particularly unfortunate to use expressions such as "shrewishly" (p. 75) and "bitchiness" (p. 77). There is a danger that such clumsiness may distract some readers from utilising the book to the degree it deserves.

This may be compounded by Skynner's clearly stated view that for some families it is optimal for the father to accept ultimate responsibility and authority for all important matters. What he is referring to is something which most marital and family psychotherapists are familiar with, particularly in relation to working with the more severely disturbed relationships and chaotic families: that is, the lack of structure, boundaries and authority which such families display. The therapeutic solution is of course the development of benevolent boundaries and authority, but there is no reason why this should necessarily be in the domain of the male. Most appropriately, this should be carried jointly by the parental couple in the case of a family, and by both spouses in the case of a marriage. Without denying appropriate differentiation, clinical experience demonstrates quite clearly that it is the capacity to share power and authority that produces healthy marriages and families.

The final thought is simply one of interest. There has recently been a lot of interest, at least among those more inclined towards a psychoanalytic framework, in Bion's concept of container-contained (Bion, 1962, 1967), developed out of Klein's concept of projective identification (Klein, 1946). Bion's model of containment suggests how personal relationships can be so beneficial and therapeutic. The other's capacity to be sensitive to, process and make some sense of tensions and anxieties evoked by the self, all usually unconsciously, allows the tensions and anxieties to be experienced less persecutorily. It also allows for the self to internalise the notion that such containment is possible and so begin to better manage inevitable feelings of conflict and fear.

This framework is very useful for thinking about the nature of marital and family interaction; about what the marriage and the family naturally fulfil for the individual members. It also offers a model for psychotherapeutic intervention. It may be that when a couple or a family seek psychotherapeutic help, it is because their natural containment capacity has broken down; the psychotherapist is sought to offer a temporary containment in the psychotherapeutic relationship, which allows the now unmanageable tensions and conflicts to be reflected upon.

Inherent in Dr Skynner's book is the attempt to think about what is happening between the couple in a marriage or between family members. His personal openness, and his willingness to use whatever concepts and theories prove of value, suggests that he would find Bion's framework at least familiar.

When I started to think about writing this review, I wrote to Dr Skynner to tell him of my project. He wrote back a very generous letter of some length. I am sure that he will not mind if I quote his final paragraph:

> "... I never intended to write a book at all! At the time I began, it was impossible to get American text books on family therapy in Britain, and I decided to write a long paper or pamphlet of about 50 pages for the seminars I was doing then. However, 50 became 100, 100 became 200, 200, 400 and even then I realised it was all just an outline summary of what I had to say".

I, for one, am very pleased and grateful that Dr Skynner wrote this "outline summary". It proved substantial food for thought and reflection when published in 1976, and still does today. It remains an introduction of some substance and I for one continue to use it, not uncritically, and to recommend it. The publishers are quite right to keep it in their lists and to republish it.

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Book Reviews

Editor: Sidney Crown

Chronic Pain: Volume 1. By THOMAS MILLAR. Madison: International Universities Press. 1990. 361 pp. $50.00.

Chronic Pain: Volume 2. By THOMAS MILLAR. Madison: International Universities Press. 1990. 883 pp. $65.00.

This publication is in two volumes, each of two parts. Throughout, not only is the multidisciplinary approach to the management of chronic pain emphasised but also the many facets involved in the establishment of pain and suffering. There is generally a lean toward psychological management (most of the 34 contributors are from departments of psychiatry or psychology) perhaps representative of the direction in which chronic pain management is progressing.

Part 1 – "The nature of pain" – includes a chapter reviewing current concepts of pain mechanisms and treatment and gives outlines of pharmacological and non-pharmacological methods of pain management. The chapter on economic, ethical and psychosocial considerations produces some interesting statistics (back pain costs the USA $24 billion per year [1982 figures]) but obviously relates to the USA rather than Europe. There are so many flaws in the studies of the contribution of ethnic factors to pain that the conclusion to this chapter would have been sufficient information. The chapter on litigation and compensation (an area of some considerable controversy) looks at legal issues, practical problems and their psychological effects, but once again is really only applicable to the USA.

Part 2 – "Diagnostic issues in chronic pain" – also looks at management of the chronic pain patient. There is a chapter on the assessment of the chronic pain patient using the Minnesota Multiphasic Pain Inventory which has been used extensively in an attempt to identify patient sub-groups and predict success of treatment programmes. The personality profiles ascribed to chronic pain patients have, however, been challenged. There is a good, balanced chapter on the management of patients with cancer, although again diagnostic issues are barely touched. This chapter gave an outline of the management of patients with cancer pain, indicating the usefulness of psychological approaches and discussing the limitations of destructive nerve blocks.

Part 3 – "Multiple strategies in the treatment of chronic pain" – includes a chapter on biofeedback and hypnosis. Although a number of encouraging case studies are described, biofeedback has generally not been found to confer any greater benefit than relaxation alone and its precise role remains unclear. The following chapters provide further interesting case reports but there is a certain amount of repetition particularly on the use of cognitive and behavioural aspects of chronic pain management.

Part 4 – "Perspectives in chronic pain" – includes a chapter "Understanding paediatric pain" which looks at psychological development, assessment and management of paediatric pain. The importance of taking into account the developmental status of the child is stressed and once again the importance of the multidisciplinary approach. Areas for further research are indicated. The chapter on the role of the clinical social worker was of interest since in the UK probably few pain clinics yet have the benefit of a social worker as part of the team. This is surprising in view of the frequency with which social and family problems are reported to be intimately connected with pain problems and this chapter perhaps gives us some guidance for the future. Part 4 finishes with a short chapter – "Chronic pain and the geriatric patient" – again a topic that attracts surprisingly little attention in view of the age spread of our population.

If you are happy with the American style (words like operationalisation spring to mind) and the repetition of certain aspects, then these volumes provide an overview to multidisciplinary pain management with an emphasis on a psychological approach.

DAVID G. GAYLARD, *Consultant Anaesthetist, Pain Management Clinic, Royal Devon and Exeter Hospital, Exeter*

Advances in Psychosomatic Medicine – Vol. 20: Methods in Teaching Consultation–Liaison Psychiatry. Edited by M. S. HALE. Basel: Karger. 1990. 144 pp. £42.60.

Much of the justification for liaison psychiatry has been its educational potential. Indeed, in the United States, the subjects rapid expansion during the 1960s and early 1970s was due to special Government funding in order to improve the training of medical students in psychological and social issues. Awareness of the importance of teaching and training has encouraged many excellent teachers, especially in North America. It has also meant that many other psychiatrists who work in general hospitals have been both concerned about how to integrate their teaching with medical training and have often been dismayed at the slowness of progress.

It is relatively easy to define the broad aims of liaison psychiatry in teaching the psychological aspects of medicine and surgery to medical students and to other general hospital staff, and to training psychiatrists in a special interest area which requires special knowledge and skills. It is much more difficult to know how we should do this. Part of the problem is that liaison psychiatrists have not yet clearly defined the special problems, clinical skills and treatments appropriate to the general hospital setting; another obstacle is the practical difficulties of setting up regular teaching within other medical units. Liaison psychiatrists require the time and the appropriate access to students, as well as the support and collaboration of colleagues. It remains rare for psychiatrists to be able to teach together with physicians and surgeons who are willing to reinforce the importance of psychological skills.

This latest book, the 20th volume in a now well established series has the right title and the right aims. Does it tell us what we want to know? The answer must be equivocal. It is relatively short, and surprisingly, three of the eight chapters have nothing to say about teaching methods. A good introductory chapter (Helz & Thompson) surveys the general approaches to consultation–liaison psychiatry, most of which are dependent on much greater resources than are available in most British units. Two chapters provide useful accounts of interviewing (Bird & Cohen-Cole) and the teaching of behavioural medicine (Gallagher).

It is a book to consult for valuable sections and for references, not an essential reference or practical guide.

RICHARD MAYOU, *Clinical Reader,*
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The Work and Play of Winnicott. By SIMON GROLNICK. Northvale, New Jersey & London: Jason Aronson. 1990. 232 pp. $25.00.

In a wonderfully Winnicottian manner Grolnick includes in his Preface to this work, an account of his 'unacknowledgements'. This is a playful reference to all those colleagues and teachers who resist change and new ideas and are enslaved by orthodoxy. It is also a good joke.

Winnicott was a paediatrician, psychiatrist and psychoanalyst combined. The beauty of his ideas are in their common sense and he was a theoretician and clinician with a lot to say to the general psychiatrist. It is not necessary to be a devotee of an exclusive psychoanalytic model to find value in his ideas, particularly in understanding the clinical situation.

The body of this book is an exploration of Winnicott's ideas, capacity to play and therapeutic originality. Grolnick traces Winnicott's development involving the incorporation of scientific principles derived from his medical training with a psychoanalytic interest tinged with poetic creativity. But the Winnicott of this book is also very human with foibles and idiosyncrasies. This model gives permission to clinicians to develop their own style and 'true self' within the theory.

In a limited way, Grolnick describes Winnicott's own development, tracing his evolution from Freud & Klein to a unique position of his own. Possibly driven by his own experiences in a female-dominated household, Winnicott spent a considerable time observing mothers with their infants. His paediatric practice was the creative setting for his theories on 'the good enough mother', 'holding environment', 'transitional object' and 'false self', which are Winnicott's major contributions to understanding human nature and interaction. Grolnick explores each concept clearly and devotes separate chapters to the Winnicottian mother/baby, to the developmental line of self, to object relatedness and to creativity. While Grolnick's prose is fluent here, it becomes turgid when discussing the more secret areas of Winnicott's own personality.

Winnicottian theory is very hopeful, seeing great value in patients' aggression as a motive force. Like the Winnicottian mother, the Winnicottian therapist learns to value the power of patients' hate. Thus the patients' true self gains confidence and all aspects of the self are allowed full expression and are utilised in personal growth. It is this hate or energy that spurs one on towards the outer fringes, creative absurdities or ludicrous possibilities where a livelier being exists. In a sense this happened to Grolnick too. While the middle section of the book is an excellent account of Winnicottian theory, it is a bit lifeless. It is in the end section, where Grolnick allows himself to play while describing Winnicott at play, that the initial humour returns and in a more lively Winnicottian vein, Grolnick combines humour and play with the serious business.

An interesting and exciting book, excellent reading for those unfamiliar with Winnicott. It is a useful starting point for moving onto Phillips' *Winnicott* (1988, London: Fontana) which is an analysis of the more complex aspects of Winnicott's theory.

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Mutism. By YVAN LEBRUN. London: Whurr Publishers. 1990. 124 pp. £18.95.

Mutism, meaning the absence of speech, has a long history preceding its adoption as a medical symptom.

Viewed through non-medical eyes, mutism has been valued as silent prayer and reviled as dumb insolence. Modern medicine has identified various 'organic' brain lesions associated with loss of speech, so that some of those who were once thought mute might now be considered aphasic. However, there remain individuals whose loss of speech cannot be explained by structural damage to the speech organs or the brain. When such behaviour is perceived to be under voluntary control it is generally outside the remit of doctors, except for elective mutism in children which may be referred to child psychiatrists. When mutism is perceived to be involuntary, then 'functional' psychiatric disorder such as hysteria or catatonia may be inferred.

Yvan Lebrun, Professor of Neurolinguistics in Brussels, divides his book into a study of 'functional' and 'organic' mutism. At first this seemed a little strange, as I had never considered that the similarity of the mouth and vagina could account for the predominance of mutism in women, or that laryngectomy, motor aphasia and pseudobulbar palsy were causes of mutism. It then became clear that 'functional' mutism was being described from a Freudian inspired, psychoanalytic perspective and 'organic' mutism from a strict neurological perspective.

What seemed to be missing from this account was the perspective of contemporary neuropsychiatry. There was almost no mention of the major psychiatric disorders which can give rise to mutism seen in catatonia and stupor. No attempt was made to consider how the pathogenesis of mutism in psychiatric disorder may result from disturbed brain function. For example, elective mutism in children has been linked to a lowered threshold of limbic/hypothalamic arousal resulting in the inhibition of voluntary or propositional speech. Similarly, the distinction between catatonic and akinetic mutism becomes increasingly blurred as more is known about the involvement of sub-cortical structures in psychotic disorders.

Professor Lebrun provides charming literary and historical references to mutism. However, this book is firmly in the dualist tradition, and as such is unable to incorporate the increasing evidence suggesting the neurobiological basis of 'functional' mutism.

CHRIS HOLLIS, *Senior Registrar in Child and Adolescent Psychiatry, The Maudsley Hospital, London*

Management of Normality. By ABRAM DE SWAAN. London: Routledge. 1990. 234 pp. £9.99.

Subtitled *Critical Essays in Mental Health and Welfare*, this book examines how definitions of 'normality', reinforced by reductionist research methods are used to justify 'protoprofessionalisation', a process whereby everyday problems are increasingly seen as the province of specialists. It is argued that society is, by this means, shielded from the suffering, and encouraged to avoid struggling with the political, moral and social issues inherent in the distress of others. De Swaan further dissects the complexities of the relationship between 'helper' and 'help seeker', their interdependency, and their inherent conflicts of interest. Processes whereby the various professions stake out and defend their developing territories are examined.

The first section explores these ideas in relation to the medicalisation of extensive areas of life, leading to an increasing preoccupation with physical health and diet rather than, for instance, character formation and social conflict. The existence of a covert agreement between doctor and patient to discuss certain issues and not others is well illustrated in a chapter on "Affect management in a cancer ward". This examines in detail the defensive strategies used to protect both staff and patients from being overwhelmed with anxiety at their shared predicament.

The second section focuses on the complexities of the relationship between psychotherapist and client, and the ground rules and mystique inherent in the process which, it is argued, serves to allocate power and control to the therapist. A final section examines the social contexts of agoraphobia, jealousy, intimacy and the survivor syndrome.

By exploring 'normality' through the dual perspectives of sociology and psychotherapy, De Swaan has produced a thought provoking, densely argued and important book which raises issues which deserve to be widely considered and debated, particularly by those in the helping professions. It is well produced and extensively annotated, although a larger typescript would have made it more comfortable to read.

MARGARET R. HILTON, *Consultant Clinical Psychologist, St George's Hospital, London*

Eclecticism and Integration in Counselling and Psychotherapy. Edited by WINDY DRYDEN and JOHN C. NORCROSS. Loughton: Gale Centre Publications. 1990. 88 pp. £6.95.

This slim volume is a reprint of four articles which originally appeared in *The British Journal of Guidance and Counselling* in 1989. The first chapter by Norcross & Grencavage briefly introduces Arkowitz's three main ways of trying to integrate the numerous and diverse forms of psychological treatments. The three approaches are; theoretical integration, (systematic) technical eclecticism, and common factor integration. Theoretical integration is concerned with combining various theories into a more comprehensive, superordinate conceptual framework; technical eclecticism is based on the atheoretical and pragmatic use of different techniques which have been empirically shown to be effective; and common factor integration concentrates on components which are not specific to any particular therapeutic approach.

In the second chapter, Lazarus (the proponent of multimodal therapy) advocates technical eclecticism, which employs any technique that has been shown to be effective. Explanations for the effectiveness of these methods is sought in Bandura's social and cognitive learning theory and any attempt at theoretical integration is believed to be premature. In view of the summary dismissal of the common factor approach by Norcross & Grencavage and their evidence for the preference of eclectic therapists to call themselves theoretical integrationists rather than technical eclectics, it is somewhat surprising to find that Beitman in the subsequent chapter, entitled "Why I am an integrationist (not an eclectic)", sees himself as a common factor, rather than a theoretical integrationist. It would have been more consistent and enlightening if this contribution had provided an illustration of theoretical integration. Nonetheless, Beitman's model of psychotherapy, which consists of four stages analysed in terms of six elements, deserves wider and closer scrutiny.

The final chapter by Messer appropriately points out some of the difficulties in using therapeutic approaches based on different theoretical viewpoints. The important issues raised in this brief volume will hopefully stimulate a more considered and rigorous examination than that provided here.

DUNCAN CRAMER, *Lecturer in Social Psychology, Loughborough University, Loughborough*

Object Relations Group Psychotherapy: the Group as an Object, a Tool and a Training Base. By RAMON GANZARAIN. Madison: International Universities Press. 1989. 1363 pp. $40.00.

The title of this book is a succinct summary of its contents and intentions. The book describes the application of the British object relations theory to the conduct of groups, mainly it seems, for the benefit of an American audience which is less familiar with this than its British counterpart, concentrating particularly on contributions of Melanie Klein and of Bion.

The first section describes some of these concepts and argues their applicability to group work. It aims in particular to demonstrate the power of the model in both eliciting and containing primitive and psychotic processes within a group setting. The second section selects some notably difficult technical problems – incest, borderline problems and hypochondriasis, to demonstrate the effectiveness of a group run on object relations lines in dealing with them. The third section makes a powerful case for the training of medical students in psychiatry to include the participation in a group, showing that those students who do take part in such an experience have a sounder theoretical and practical grasp of psychodynamic principles as well as deriving considerable personal benefit and being freer of problems later on in their careers. These chapters alone are important although written in the mid 1950s before the author was acquainted with object relations theory.

This book makes an important contribution, despite suffering from various defects. I doubt whether the rapid run-through of object relations theory or of Bion's theories would be intelligible to someone not already conversant with them, which probably makes the book inaccessible to the average inceptor and to many psychiatrists. Many of the chapters have been published previously in journals which makes for a somewhat jerky read with some rather irritating repetition. I often felt that the most powerful argument was for the efficacy of object relations theory rather than of the group process, particularly in relation to the chapters on incest and hypochondriasis. In contrast, the chapters that argue for the teaching of psychodynamic psychiatry in groups made a cogent case for the group process itself without reference to the object relations component which had not yet become available to the author. Nonetheless these two components do come together effectively, particularly in the description of transference and counter transference processes and in the elucidation and containment of primitive processes in groups whether of patients or of non-symptomatic, 'well' students.

A book therefore perhaps for the interested, adventurous or specialist psychiatrist. The rest will probably need it filtered through their specialist colleagues. But it would be a pity if the message did not get through.

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Brief Therapy: Myths, Methods and Metaphors. Edited by JEFFREY K. ZEIG and STEPHEN G. GILLIGAN. New York: Brunner/Mazel Publishers. 492 pp. $42.50.

This book is based on the Fourth International Congress on Ericksonian Approaches to Hypnosis and Psychotherapy, held in San Francisco, California in 1988. The title is, therefore, somewhat misleading for those readers expecting a broad overview of brief therapies. Although there are contributions from such notable brief therapists as Ellis and Sifneos, with a particularly good chapter by Strupp on the development of a psychotherapy training programme, the book is predominantly concerned with Ericksonian therapy.

Many different variations are described, including 'redecision therapy', 'ecological therapy', 'therapy is what you say it is' therapy, etc. Need I say that this is a very American book! For those unfamiliar with Ericksonian therapy, the book is filled with many clinical vignettes which graphically convey the positive style and directness of its approach. There is a marked absence, however, of any kind of formal evaluation of its efficacy. This is particularly frustrating, as the reader is repeatedly bombarded with clinical accounts of patients with longstanding symptoms, unhelped by previous analysts, who then begin Ericksonian therapy and are, of course, cured within a few weeks. It would have been reassuring to read about a patient who could not be helped by this kind of approach!

The opening chapters of the book are spoilt by repeated, unnecessary criticisms of psychoanalysis, and little factual information regarding Ericksonian methods is presented.

The next sections, however, are much more balanced and interesting, although the chapters on metaphors were rather disappointing. The section on family therapy is particularly enthralling. It includes an entertaining account by Papp of how a debate amongst therapists, regarding solutions to a family problem, can become a therapeutic tool, if the debate is carried out in the presence of the family themselves.

The book is an unashamed homage to the late Milton Erickson, clearly a remarkable man, who generated great affection, loyalty and regard from those who knew him. The most interesting aspects of the book are inevitably those personal memories and insights given by many of the contributors (including three of his children) of Erickson as therapist. This book is a must for the Ericksonian devotee, but is unlikely to be of interest to many psychiatrists or psychotherapists in the UK.

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Relapse Prevention for Addictive Behaviours: A Manual for Therapists. By SHAMIL WANIGARATNE, WENDY WALLACE, JANE PULLIN, FRANCIS KEANEY and ROGER FARMER. Oxford: Blackwell Scientific Publications. 1990. 205 pp. £12.95.

The art of packaging an idea to capture the public imagination is not only the advertising copywriters' skill. In the midst of the 'cognitive therapy revolution' relapse prevention has caught the imagination of the growing army of addiction workers.

The central idea of relapse prevention has been to focus treatment of alcohol and drug problems and other behavioural addictions on the maintenance of behaviour change or, as the originator of relapse prevention, Alan Marlatt writes in the foreword, to "educate clients in the art of autoregulation".

Teaching people to stay drug-free has been the role of Alcoholics Anonymous (AA) for decades, so one should ask what makes relapse prevention different. The authors of this book suggest that relapse prevention focuses control on the individual while AA is based on a medical model that wrests control from the individual. In many ways relapse prevention may be seen as the key elements of the AA strategies recast with the theoretical underpinnings of social learning theory. The availability of relapse prevention widens the range of treatment options and increases the possibility of tailoring treatment to individual need.

The authors of this book provide an overview of the theoretical concepts underlying relapse prevention, as well as detailed descriptions of their own method of applying this approach to group therapy. They provide details of all their own data sheets and evaluation forms which could be useful for people wishing to apply such an approach.

The book describes six weekly group therapy sessions with a detailed programme for each. The sessions are for people who have stopped or controlled their drinking or drug use and aim to facilitate the maintenance of this change. They aim to teach people to identify high risk situations and to develop alternative coping strategies. Other areas such as relaxation, anxiety, meditation, assertiveness, problem solving, depression and life style balance are covered.

Overall the manual outlines a well structured and detailed programme of relapse prevention focused group psychotherapy. Clinicians embarking on relapse prevention will find many helpful, detailed and practical points in this manual.

MICHAEL FARRELL, *Research Senior Registrar, Addiction Research Unit, Institute of Psychiatry, London*

The Genetics of Mood Disorders. By MING T. TSUANG and STEPHEN V. FARAONE. Baltimore: The Johns Hopkins University Press. 1990. 220 pp. £29.00.

The aim of this book appears to be to summarise most genetic studies of mood disorders from their earliest days to the present. The format is traditional, with a chapter on diagnostic and methodological issues, followed by sections on family, twin and adoption studies. Having demonstrated the heritable nature of mood disorders, the authors then discuss modes of transmission, linkage and association studies, and lastly biological markers. The final chapter attempts to draw conclusions from the preceding text, and discuss the implications of the research to date. Overall, the authors have fastidiously covered almost all areas of genetic investigation and present their review of the literature in detail. The text may therefore serve as an excellent base which the interested reader can further develop.

Unfortunately, the style is a bit soporific and the book starts with a chapter that could well deter all but the most dedicated from progressing further. The authors, while successfully arguing that mood disorders may encompass syndromes heterogeneous in aetiology, grossly over-cite studies to support this rather modest and uncontroversial claim.

Once this hurdle has been overcome, one moves on to the discourse proper. All the chapters are similar in style, starting with a useful introduction to the rationale of the study designs to be discussed and some mention of their limitations and pitfalls. There then follows a thorough enumeration of the studies, with a brief description of each, followed by a general summary.

The introductory aspects of each chapter are variable in quality, being particularly good as related to family, twin and adoption studies, but poorer as pertains to models of transmission and marker studies. For the latter types of study this is a major deficit when trying to make sense of findings which, as a rule, are conflicting. An irritating feature of the introductions is the presence of equations which are not derived mathematically or explained in English. Although mathematical derivation is probably beyond the scope of this book, the failure to explain the equations in common sense terms is liable to reduce the reader to the role of spectator.

The substance of each chapter gives a review of individual studies pertinent to the title of that chapter. The result is that an immense amount of information is presented, but with a relative paucity of integration and generalisation, ensuring that the text is enlightening, if somewhat dry. However, although the style may be off-putting, both the raw data and the essences thereof are present, albeit in separate parts.

In short, the main asset of this book is a detailed breakdown of an immense number of publications covering the full range of genetic investigations into mood disorders. It also has useful introductory discussions of the methods of family, twin and adoption studies but is poorer in other aspects, particularly studies of linkage and association. Summation of the data is a relatively minor feature of the book, and therefore it is not particularly recommended to the general reader. Psychiatric libraries, however, would be providing themselves with a worthwhile source book.

MICHAEL C. O'DONOVAN, *MRC Research Fellow, University of Wales College of Medicine, Cardiff*

Current Concepts of Suicide. Edited by DAVID LESTER. Philadelphia: The Charles Press. 1990. 236 pp.

This volume is intended to provide a summing up of where we stand in the field of suicide research. Suicide is an area where there is an obvious interface between many different academic disciplines, and this volume contains contributions from psychiatrists, psychologists, sociologists, and anthropologists, each writing from the point of view of their discipline.

Contained in the book, therefore, are many different approaches to the study of suicide. Two chapters looking at the biology of suicide are extremely well written and easy to understand. The putative role of serotonin is placed in perspective with a plea for increased precision in the methodology of behavioural measurements. One chapter focuses on the work of Durkheim, who has had a tremendous influence on the study of suicide from the point of view of sociology. This is brought up to date with a useful account of the current debates in the world of sociology concerning Durkheim's theories. There are chapters reviewing the role of the media in suicide and also public health issues connected with suicide. One point made in the latter contribution is the lack of awareness in this country about the impact that stricter emission controls on car exhausts have had in reducing deaths from suicide due to carbon monoxide poisoning. Additionally, there is an intriguing account by an anthropologist of the concept of 'revenge suicide', whereby women in some cultures are able to assert some control over the society in which they live by the act of suicide. Another useful review is a critical analysis of using the ecological approach in studying suicide.

This book offers psychiatrists the chance of reading about some of the developments in other academic fields that relate to suicide. A common failing of some American-edited volumes is avoided in that the authors of the different chapters come not only from the United States but also Canada and Europe. There is only an odd chapter or two that is poorly written with comments on research of dubious value. The diverse topics covered and overall quality of this volume result in a stimulating book from which I was able to learn a great deal.

CHRISTOPHER VASSILAS, *Lecturer in Mental Health, University of Bristol*

Emotions and the Dual Brain. Edited by G. GAINOTTI and C. CALTAGORONE. Heidelberg: Springer GmbH. 1989. 270 pp. DM98.00.

Charles Darwin's claim that emotional expressions are part of man's biological inheritance seems only recently to have been rediscovered. This rediscovery has been fuelled by interest in the right cerebral hemisphere, which many believe to be as dominant for emotional behaviour as is the left hemisphere for linguistic functions. This collection of essays was based on a conference in honour of an Italian physiologist, Giuseppe Moruzzi. Much of the writing reflects the neurological bias of the research presented, such as chapters by Doty on the anatomical substrates of emotion and connections between the two hemispheres, whereas chapters by Gainotti and Etcoff look at different emotional disturbances resulting from brain lesions in humans. Latter chapters take on a more cognitive approach with a chapter by Tucker from Oregon which looks at possible brain abnormalities underlying affective disorder.

The concluding chapter is by Kinsbourne in which he attempts to pull together many of the preceeding strands. There is food for thought here for psychiatrists who glibly speak of 'biological' symptoms in depression. In his final paragraph Kinsbourne admonishes those naive enough to localise emotional disturbances to areas of the brain, outlining instead how cognitive rearrangement necessitated by lesion-induced deficits elicits emotional changes, and it is this dynamic model which promises most in future research.

ANTHONY DAVID, *Senior Lecturer, Institute of Psychiatry, London*

The Hamilton Scales. Edited by PER BECH and ALEC COPPEN. Berlin: Springer Verlag. 1990. 94 pp. £21.00.

This slim volume contained many surprises for this reviewer, who has been using the Hamilton Rating Scale for Depression (HRSD) for over a decade. A number of the articles are excellent, in particular that by Berrios and Bulbena-Villarasa. But overall, the book is a celebration of Max Hamilton rather than a serious attempt to put him or the development of his scale in a historical context.

However, a number of the papers in this collection point the way. For example, Zitman *et al*, in a survey of uses of the scale, found that only one respondent was actually using the scale they claimed to be using. There were a large number of differences in the versions actually used, with versions containing anything from 17 to 25 items. One version used 1–3 or 1–5 point scales, so that the minimum possible score was 17 – which for most people translates as moderate depression. Such findings seriously compromise what Paykel has suggested is a principal use of the scale which is that, rather than being a good measure, it functions as a common language. Scores of 14, 17 or 26 are shorthand for particular clinical conditions. This is a property that no other scale has achieved despite many of the others having greater internal consistency and sensitivity to the effects of antidepressants.

Another appealing paper, by Pull, cites the complete indifference with which the scale was first greeted, and its subsequent transformation to the point where it is considered to be an indispensable research tool. One of the lone voices arguing that this transformation was unwarranted appears to have been Hamilton himself, who saw the scale as a method of assisting clinical judgement rather than a means of subverting it. He was aware that quantification and statistics would impress those who do not understand or who do not want to understand.

One of the critical questions for the future must be whether other methods for evaluating psychotropic drugs can be devised, as at present the Hamilton Scale is almost too loved by drug companies. In pointing out issues such as this, this book can give food for thought to all of us regarding the probabilistic and essentially arbitrary basis of much of current psychiatric practice and thinking, while we wait for the definitive treatment of Hamilton and his scales.

DAVID HEALY, *Senior Lecturer in Psychological Medicine, North Wales Hospital, Denbigh, Clwyd*

A Casebook in Psychiatric Ethics. GROUP FOR THE ADVANCEMENT OF PSYCHIATRY COMMITTEE ON MEDICAL EDUCATION. New York: Brunner/Mazel. 1990. 128 pp. $21.95 (hb), $14.95 (pb).

I approached this book with mixed feelings – would it stretch me intellectually with philosophical riddles or frustrate me with an inadequate understanding of the realities of psychiatric practice? In the event it did neither. It simply presents a series of ethical problems in the form of clinical vignettes and invites the reader, or a group if it is used for teaching as suggested, to consider the issues raised.

The 17 case histories, which easily cross cultures from the USA to the UK, illustrate five themes. The first is consent, but with the incorporation into British legal systems of the consent of detained patients surely no psychiatrist can be unaware of the issues involved. The section on paternalism addresses compulsory admission and treatment but ignores the intriguing question of why paternalism is used as a term of abuse against professionals but never as such against fathers.

The most interesting case arises in the section on relationships with colleagues and concerns the junior's dilemma when his or her clinical judgement is at odds with the supervising senior's – the most interesting case but the least easily resolved. Sexual attraction towards patients has rarely been acknowledged in the British literature (excepting a leader in the *Journal of the Royal Society of Medicine* last year). In the final section the dilemma facing a doctor being pressured into admissions for financial rather than clinical reasons may be with us sooner than we would like in the light of present changes in the National Health Service.

I was left thinking that this book was not for me – it does not raise any issue more complex than those I meet every day at work. I would be as likely to pause on a ward round to teach on such topics as I would on the niceties of drug treatment, or on an explanatory psychodynamic formulation or on the influence of social factors on a patient's prognosis. That being said, this is a modestly priced and well-written book and the tutor who is struggling to help his trainees grasp ethical issues may find it useful support for his efforts.

DAVID TAIT, *Physician Superintendent, Murray Royal Hospital, Perth*

Children with Down Syndrome: A Developmental Perspective. Edited by Dante Cichetti and Marjorie Beeghly. Cambridge: Cambridge University Press. 472 pp. £35.00 (hb), £15.00 (pb).

My difficulties with this book began with the title. Syndromes are normally described by the name of the person who described them in the genitive, therefore Down's Syndrome and not Down Syndrome; in this case the grammatical alteration felt particularly unfortunate. Then, in the first page, I was faced with 24 references, and this did not get much lighter further into the text. The rhythm of the text kept getting broken, and the heavily jargonised language made reading copious, with the possible exception of the chapter on conceptual development by Mervis. Twelve of the thirteen chapters are founded on observation-based research, but avoid any speculation as to the usability in the clinical context of the insights which they promote; only the last and briefest chapter addresses intervention, and even then in the detached style of a review. There is a recurring assertion throughout the book that better understanding of developmental issues will influence practice, but the book concerns itself exclusively with the better understanding, not with the influences on practice; this makes it static rather than dynamic, and seriously affects its clinical relevance.

The thoroughness of the reviews and the long reference lists would certainly admit a place in the reference section of academic libraries and make it a valuable source book for researchers, but as for the claim on the jacket that it will appeal even to parents, it must be referring to researcher parents. The book is not unreasonably priced, particularly the paperback version.

Aris Ambelas, *Consultant Child Psychiatrist, Leicestershire Health Authority and Medical School, Leicester*

Child Development and Personality. By Paul Henry Mussen, John Janeway Conger, Jerome Kagan and Aletha Carol Huston. London: Harper & Row. 1990. 700 pp. £13.95.

Of all the standard American texts on child development this is the grandparent. Now into its seventh edition, it still sells over 100 000 copies a year, and is used by more college courses than any other similar book. Over the years it has adapted well to changing demands. While retaining the conventional format, starting with the pre-natal period and concluding with adolescence, it has incorporated the shifting emphases of theory and practice, and remains a lively and readable book.

In this latest edition, several topics have new or considerably expanded coverage. In the first section, important information about behavioural genetics and hazards in pre-natal development is discussed. In the chapter on infants, recent knowledge derived from neuroscience about cognition and emotion is presented, together with information about cross-modal perception, temperamental differences in sociability and inhibition, and a current assessment of daycare. An entire chapter has been devoted to the transition from infancy to early childhood – a period of development that has until recently been virtually ignored.

In the area of childhood, challenges to Piaget are well documented, together with up-to-date approaches to language acquisition and the development of cognitive skills. A new chapter on government policy and its effects on family life has been included, and in the adolescence section there is increased emphasis on topical issues, such as teenage pregnancy and parenting, drug abuse, and affective disorders.

Particularly interesting are the three text boxes inserted in each chapter to describe social issues, case studies or important research. Topics covered include the developmental risks of children with sex chromosome abnormalities, research on parent–infant bonding, a case study of a child who was isolated from human language until age 13, an autobiography of a black child growing up in the United States, research on only children in China and research on the effects of employment during secondary schooling.

Sad though it is, it has to be acknowledged that there is no European competitor to this volume with quite the same comprehensive coverage. Although essentially an undergraduate text, it remains pre-eminent in the field of child development.

John C. Coleman, *Director, Trust for the Study of Adolescence, 23 New Road, Brighton, Sussex*

Sainsbury's Key to Psychiatry. (4th edn) By M. J. Sainsbury and L. G. Lambeth. Chichester: John Wiley and Sons. 1988. 519 pp. £15.95.

This is a medium-sized general psychiatric text book, presumably marketed as a moderately comprehensive outline of general psychiatry to suit the postgraduate requirements of trainees. In general its scope is about right and anybody who digested the majority of its contents would probably have little difficulty with the MRCPsych examination. The bibliography is just about right for its intended readership and it has a useful ICD glossary at the back.

However, the book does have a few flaws and drawbacks. For instance, it is riddled with spelling errors, e.g. 'multi-infa*r*et' dementia' and 'Tricycli*d*' (sounds like a malevolent plant from a John Wyndham novel). The book is written in a somewhat woolly, anecdotal style with examples of various phenomena being illustrated by long-winded accounts from the authors' own clinical practice. There is also an irritating trend to tautology, e.g. "tyramine in food that is eaten". More seriously, the sections outlining pharmacological methods of treatment are seriously flawed and could lead to instant failure in an examination or have deleterious clinical effects. The examples are numerous, for instance it is suggested that thirst and polyuria due to lithium might be treated with chlorothiazide; that phenothiazines are useful in alcoholic delerium tremens, or that oral chlormethiazole is the first choice in controlling the DTs. The illustrations are at about first year secondary school level, e.g. a line drawing of a brain, with 'limbic system' pointing to somewhere above the corpus callosum.

From a publishing stand-point the book is printed on poor quality paper, which is already yellowing and falling apart as I write this review.

It is useful to consider this book alongside other similar, general postgraduate texts and I think they all have advantages over this. The 'Oxford textbook' is the best; it is precise, comprehensive and sound. The *Essentials of Post-Graduate Psychiatry* has a stronger discursive style for the discerning trainee and a wider bibliography, and the recently published *Postgraduate Psychiatry* is an excellent and cynical attempt to flesh out the new MRCPsych syllabus with the minimum of fuss. All of these represent better value for money.

On the whole it is difficult to fault the book as I think it achieves its main aim, but I will continue to revise from, and recommend to others, the Oxford textbook.

ROBERT KERWIN, *Senior Lecturer in Neuroscience, Consultant Psychiatrist, Institute of Psychiatry, London*

Essential Psychology: Psychology Clearly Explained and Defined. By DAVID COHEN. London: Bloomsbury. 1990. 241 pp. £5.99.

Essential Psychology is effectively a dictionary of psychology, but it is rather more than a set of definitions. Thus, although the book is predictably arranged in the way one would expect of a dictionary, the alphabetical entries are more akin to an encyclopaedia. David Cohen is at pains to point out the controversies and conflict that exist within psychology. In his brief introduction, he outlines some of these issues, such as the debate over free will versus determinism. The author's intention is to "indicate critical thinking on key issues so that readers get a sense of the varying positions and indeed rows". In a book of this size, the contents are inevitably selective and Cohen seeks only to outline what he considers to be the most important terms and ideas in current usage. Broadly speaking, his selection seems like a reasonable cross-section, possibly with something of a bias towards the clinical end of the spectrum.

Entries vary from the brief one sentence variety (e.g. 'hypothalamus'), to those several pages long on more contentious subjects, such as 'consciousness'. Although most terms chosen are predictably mainstream, there is a fair sprinkling of the more esoteric. My favourite was 'orgone', which turns out to be "an entirely mythical substance that played a large part in the work of Wilhelm Reich". Apparently, it has something to do with orgasms and Reich even invented an 'orgone box', into which one could step and have a "wonderful experience"! For those who prefer a quieter life, there is no shortage of alternatives, ranging from 'CAT scans' to 'cognitive style'. There is also a selection of potted biographies of some of the 'major thinkers' in the discipline, such as Eysenck, Freud and Piaget.

Essential Psychology offers a handy and affordable resource which would be of particular value to those who are dipping their toes in before taking on something more substantial. My only gripe is that I would have liked a few more illustrations to break up the words. In spite of its attractive cover, all we are treated to is two diagrams of the brain!

ERIC BUTTON, *Chartered Clinical Psychologist, Department of Clinical Psychology, Leicester General Hospital*

Psychological Evaluations for the Courts. By GARY B. MELTON, JOHN PETRILA, NORMAN G. POYTHRESS and CHRISTOPHER SLOBOGIN. Hove: Lawrence Erlbaum Associates. 1987. 511 pp. £32.95 (US$60.00).

The authors of this book have combined their extensive experience in training lawyers, judges and clinicians to produce a comprehensive guide to the legal issues clinicians commonly address in Court.

The book covers general medico-legal considerations, issues surrounding the criminal process and non-criminal adjudications, children and families and communications with the Courts.

Each chapter is divided into sections, and lettered and numbered subsections, an organisational device which makes the content of the chapters more accessible, provides ease of cross-referencing, and facilitates up-dating through future supplements. The chapters finish with a conclusion or a summary as well as about ten bibliographies each. Following the body of the book the authors have added a valuable 22-page glossary which is followed by nearly 70 pages of notes and references grouped according to chapters. The book finally ends with a five page index which appears rather meagre in view of this very comprehensive volume.

This book in paperback, half-size, with a more extensive index and at the same reasonable price could well become the standard other books in this field are measured by. Mental health professionals working in the forensic field, as well as lawyers concerned with medico-legal issues will find it invaluable.

HEINZ ALBRECHT, *Specialist Psychiatrist, Regional Forensic Services, Auckland Area Health Board, New Zealand*

Contents of *The American Journal of Psychiatry*

May 1991 Volume 148

Special Articles

Organic unity theory: the mind-body problem revisited. *Aviel Goodman* 553
Comorbidity of attention deficit hyperactivity disorder with conduct, depressive, anxiety, and other disorders. *Joseph Biederman, Jeffrey Newcorn and Susan Sprich* 564
The psychological sequelae of therapeutic abortion – denied and completed. *Paul K. B. Dagg* 578

Regular Articles

Suicide and guilt as manifestations of PTSD in Vietnam combat veterans. *Herbert Hendin and Ann Pollinger Hass* 586
Posttraumatic stress disorder after a school shooting: effects of symptom threshold selection and diagnosis by *DSM–III, DSM–III–R*, or proposed *DSM–IV*. *Eitan D. Schwarz and Janice M. Kowalski* 592
The assessment and treatment of performance anxiety in musicians. *Duncan B. Clark and W. Stewart Agras* 598
European versus US data on the course of schizophrenia. *Joanne Marengo, Martin Harrow, James Sands and Catriona Galloway* 606
A family study of *DSM–III–R* schizoaffective disorder, depressive type, compared with schizophrenia and psychotic and nonpsychotic major depression. *Mario Maj, Fabrizio Starace and Raffaele Pirozzi* 612
Cortical magnetic resonance imaging changes in elderly inpatients with major depression. *Peter V. Rabins, Godfrey D. Pearlson, Elizabeth Aylward, Ashok J. Kumar and Kathleen Dowell* 617
Changes in brain glucose metabolism in cocaine dependence and withdrawal. *Nora D. Volkow, Joanna S. Fowler, Alfred P. Wolf, Robert Hitzemann, Stephen Dewey, Bernard Bendriem, Robert Alpert and Anne Hoff* 621
Comparison of acetorphan with clonidine for opiate withdrawal symptoms. *Francois Hartmann, Marie-France Poirier, Marie-Chantal Bourdel, Henri Loo, Jeanne-Marie Lecomte and Jean-Charles Schwartz* 627
Outcomes for cocaine abusers after once-a-week psychosocial therapy. *Sung-Yeon Kang, Paula H. Kleinman, George E. Woody, Robert B. Millman, Thomas C. Todd, John Kemp and Douglas S. Lipton* 630
Risk factors for needle sharing among methadone-treated patients. *David Metzger, George Woody, Dominick De Philippis, A. Thomas McLellan, Charles P. O'Brien and Jerome J. Platt* 636
Implications of self-reported cognitive and motor dysfunctions in HIV-positive patients. *Jean W. Wilkins, Kevin R. Robertson, Clyde R. Snyder, Wendy K. Robertson, Charles van der Horst and Colin D. Hall* 641
Expenditures for psychotropic medications in the United States in 1985. *Joseph J. Zorc, David B. Larson, John S. Lyons and Robert S. Beardsley* 644
Parents' emotional neglect and overprotection according to the recollections of patients with borderline personality disorder. *Hallie Zweig-Frank and Joel Paris* 648
Kleptomania: a report of 20 cases. *Susan L. McElroy, Harrison G. Pope, Jr, James I. Hudson, Paul E. Keck, Jr and Kerrin L. White* 652
Hypnotically induced auditory hallucinations and the mouth-opening maneuver: a failure to duplicate findings. *Eugene E. Levitt and Thomas G. Waldo* 658
Not all that moves is tardive dyskinesia. *Vikram Khot and Richard Jed Whyatt* 661

Clinical and Research Report

Imipramine treatment of methadone maintenance patients with affective disorder and illicit drug use. *Edward V. Nunes, Frederic M. Quitkin, Ronald Brady and Jonathan W. Stewart* 667

Contents of The Journal of Nervous and Mental Disease

May 1991 Volume 179

Unconscious perception: the possible implications of data from academic research for clinical practice. *Norman F. Dixon and Susan H. A. Henley* 243

Posttraumatic stress disorder following recent onset psychosis: an unrecognized postpsychotic syndrome. *Patrick D. McGorry, Andrew Chanen, Elizabeth McCarthy, Raphael Van Riel, Dean McKenzie and Bruce S. Singh* 253

Risk for suicide in schizophrenia and other psychotic and nonpsychotic disorders. *Jerry F. Westermeyer, Martin Harrow and Joanne T. Marengo* 259

Assessing the appropriateness of the prescription of psychiatric medications in prison. *Ira Sommers and Deborah R. Baskin* 267

Short- and long-term psychological status following stroke: short form MMPI results. *C. Munro Cullum and Erin D. Bigler* 274

Memory processes and hypochondriacal tendencies. *Francis T. Durso, Richard Reardon, Wendelyn J. Shore and Scott M. Delys* 279

Multidimensionality and state dependency of alexithymia in recently sober alcoholics. *Mark G. Haviland, Michael S. Hendryx, Michael A. Cummings, Dale G. Shaw and James P. MacMurray* 284

Intravenous nitroglycerine in the management of posttreatment hypertension during electroconvulsive therapy. *Jeffry R. Nurenberg* 291

Childhood sexual abuse in patients with paradoxical vocal cord dysfunction. *Michael R. Freeman, Samuel J. Rosenberg and Karen B. Schmaling* 295

Books. Field, M. A. *Surrogate Motherhood: The Legal and Human Issues*; Radelet, M. L. (ed.) *Facing the Death Penalty: Essays on a Cruel and Unusual Punishment*; Nezu, A. M., Nezu, C. M. and Perri, M. G. *Problem-Solving Therapy for Depression: Theory, Research and Clinical Guidelines*; Lerner, H. D. and Lerner, P. M. (eds) *Primitive Mental States and the Rorschach*; Ogden, T. H. *The Primitive Edge of Experience*; Chaika, E. O. *Understanding Psychotic Speech: Beyond Freud and Chomsky*; Matson, J. L. (ed.) *Chronic Schizophrenia and Adult Autism: Issues in Diagnosis, Assessment, and Psychological Treatment*; Legg, C. R. *Issues in Psychobiology*; Pearlman, A. L. and Collins, R. C. (eds) *Neurobiology of Disease*; Wertheimer, J., Bauman, P., Gaillard, M. and Schwed, P. (eds) *Innovative Trends in Psychogeriatrics*; Pepeu, S., Tomlinson, B. and Wischik, C. M. (eds) *New Trends in Aging Research*; Friedman, R. M., Duchnowski, A. J. and Henderson, E. L. (eds) *Advocacy on Behalf of Children with Serious Emotional Problems*; Vital, D. *The Future of the Jews: A People at the Crossroads?* 299

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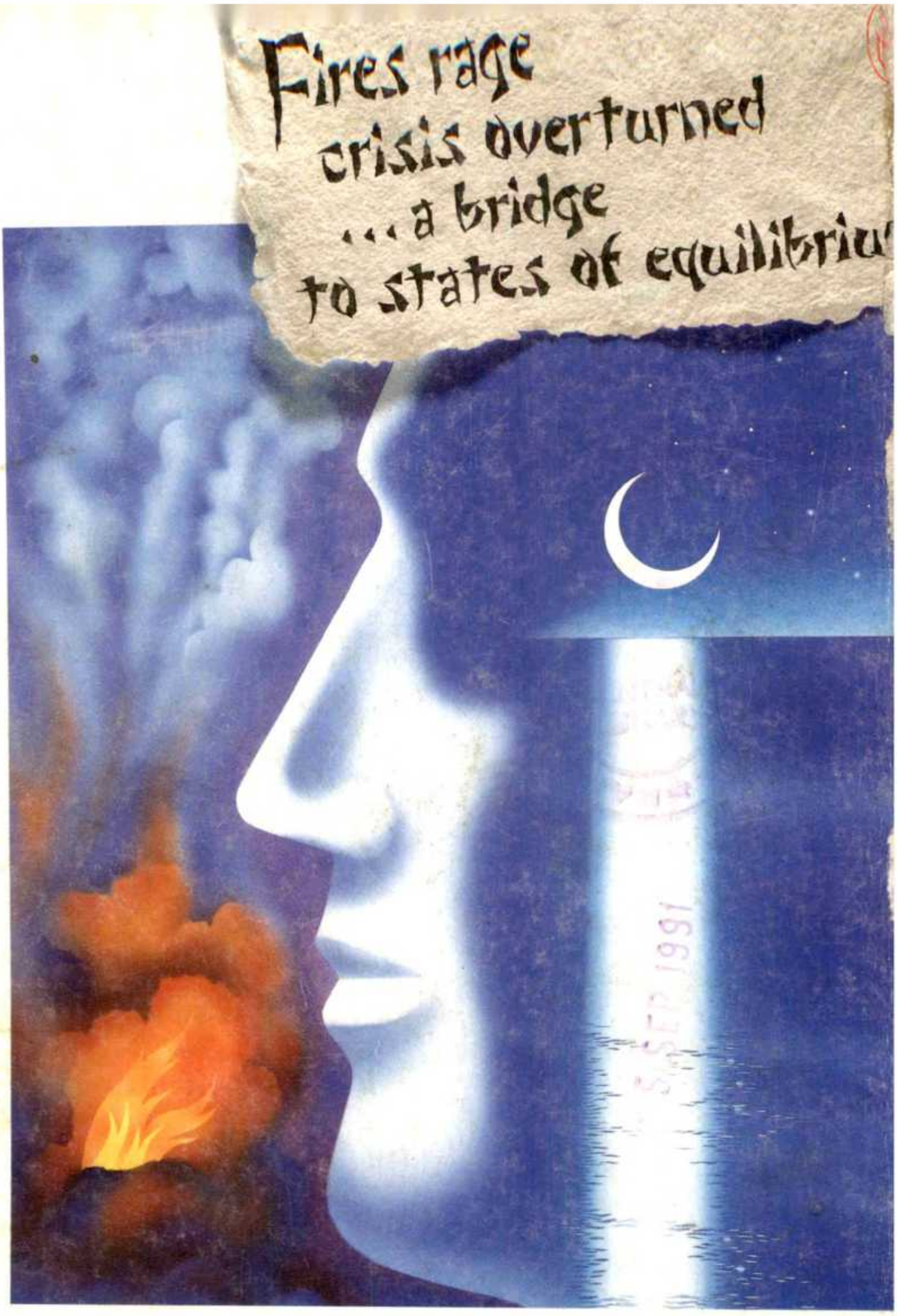

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